American Heart Journal

Vol. 37 | February, 1949 | No. 2

Original Communications

THE VENTRICULAR COMPLEX IN LEFT VENTRICULAR HYPERTROPHY AS OBTAINED BY UNIPOLAR PRECORDIAL AND LIMB LEADS

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THE electrocardiographic patterns of left ventricular hypertrophy or left ventricular strain in standard limb lead records have received considerable attention from investigators.[1-10] Less detailed attention has been paid to the pattern of left ventricular hypertrophy when using the unipolar limb and precordial leads. The typical pattern obtained by unipolar techniques has been described previously, [11-15] but the atypical ones and those showing lesser degrees of abnormalities have not been detailed adequately. The practical importance of the electrocardiographic position of the heart and of the time of onset of the intrinsic deflection of the ventricular complexes as an aid in diagnosis has been emphasized already.[11,16] The purpose of the present investigation is to evaluate the criteria, using unipolar limb and precordial leads, for the recognition of the atypical and early patterns of left ventricular hypertrophy; to determine the frequency of the characteristic changes noted by Wilson and his associates[11]; and to study the diagnostic value of the electrocardiographic position of the heart and of the time of onset of the intrinsic deflection (ventricular activation time).

METHODS AND SUBJECTS

Two hundred patients were selected whose electrocardiograms were abnormal and in whom a cardiac disorder capable of producing increased strain on the left

From the Division of Medicine of the University of California Medical School, San Francisco, Calif.
Presented in preliminary form before the Western Society of Clinical Research, Nov. 1, 1946.
Supported in part by a grant from Mrs. Albert E. Schwabacher.
Received for publication Jan. 8, 1948.

TABLE I. THE VENTRICULAR DEFLECTIONS IN UNIPOLAR LIMB AND PRECORDIAL LEADS (MEASUREMENTS IN MILLIMETERS)

LEAD	LEFT VENTRICULAR HYPERTROPHY (147 CASES)				NORMAL (151 CASES)				NORMAL—LEFT AXIS DEVIATION (21 CASES)			
	MEAN	±ST. DEV.	MIN.	MAX.	MEAN	±ST. DEV.	MIN.	MAX.	MEAN	±ST. DEV.	MIN.	MAX.
V_1												
Q	0	0	(0)		0	0	(0)		0	0	(0)	
R	1.1	1.3	0	12.0	2.3	1.5	0	7.0	1.8	1.3	0	4.5
S	13.1	5.5	3.0	35.0	8.6	4.3	2.0	25.0	8.0	3.7	3.5	18.0
T	1.5	1.84	−2.5	+5.5	0.15	1.58	−4.0	+4.0	0.4	1.32	2.5	+3.0
ID*	0.013	0.008	0	0.03	0.020	0.007	0	0.03	0.02	0.006	0	0.02
V_2												
Q	0.01	0.05	0	1.0	0	0	0		0	0	0	
R	4.0	3.4	0	18.0	5.9	3.1	0	16.0	5.0	2.9	2.0	12.0
S	15.4	6.5	0	46.0	12.7	5.3	0	29.0	10.3	4.8	4.0	18.0
T	4.86	2.75	−0.5	+13.0	5.52	3.32	−3.0	+18.0	4.08	2.68	−2.5	+9.0
ID	0.01	0.008	0	0.03	0.025	0.006	0	0.04	0.03	0.006	0.01	0.035
V_3												
Q	0.04	0.27	0	2.0	0.01	0.06	0	0.5	0	0	0	
R	9.3	6.4	0	26.0	8.9	4.3	1.5	26.0	8.6	4.0	4.0	17.0
S	10.8	6.7	0	36.0	8.8	5.3	0	25.0	7.5	4.3	3.0	16.0
T	3.53	3.27	−5.0	+11.0	5.38	2.96	−2.0	+16.0	4.67	4.37	−0.1	+13.0
ID	0.03	0.01	0	0.07	0.03	0.007	0.02	0.04	0.03	0.005	0.02	0.04
V_4												
Q	0.15	0.39	0	2.0	0.1	0.4	0	3.0	0.05	0.16	0	0.5
R	16.8	8.2	0.5	42.0	14.2	5.5	4.0	27.0	12.5	5.0	5.0	27.0
S	6.3	5.3	0	30.0	5.2	4.0	0	20.0	4.3	3.2	0	13.0
T	1.63	3.44	−6.0	+11.0	4.8	2.76	0	+17.0	4.2	2.67	−0.1	+13.0
ID	0.041	0.009	0	0.07	0.034	0.007	0.02	0.05	0.04	0.007	0.03	0.045

V_5												
Q	0.4	0.74	0	5.0	0.3	0.6	0	3.0	0.3	0.4	0	1.0
R	18.9	7.5	5.0	48.0	12.1	4.4	4.0	26.0	11.8	5.4	6.0	26.0
S	1.5	2.3	0	13.0	1.5	1.5	0	6.0	1.2	1.1	0	4.0
T	−0.28	2.93	−9.0	+7.0	3.43	1.62	0	+9.0	3.45	1.66	+1.0	+9.0
ID	0.048	0.009	0.03	0.07	0.04	0.01	0	0.05	0.04	0.007	0.025	0.05
V_6												
Q	0.45	0.76	0	5.0	0.4	0.5	0	2.0	0.4	0.4	0	1.0
R	16.4	8.9	6.0	58.0	9.2	3.6	4.0	22.0	8.9	4.1	4.0	19.0
S	0.43	1.06	0	10.5	0.6	1.0	0	7.0	0.2	0.5	0	1.5
T	−0.63	2.53	−9.0	+4.5	2.43	1.11	−0.5	+5.0	2.4	1.18	+0.5	+6.0
ID	0.049	0.009	0.03	0.08	0.04	0.01	0.02	0.05	0.04	0.01	0.03	0.05
aV_L												
Q	0.37	0.68	0	4.0	0.2	0.5	0	3.5	0.5	0.4	0	4.0
R	8.1	4.8	0	25.0	2.1	2.1	0	10.0	4.6	2.5	0.5	10.0
S	0.65	1.36	0	9.0	0.4	3.9	0	18.0	0.3	0.7	0	3.0
T	−0.51	1.37	−7.0	+2.5	0.53	1.26	−4.0	+6.0	1.0	0.81	−1.0	+2.5
aV_R												
Q	0.78	2.16	0	10.0	2.0	3.7	0	8.0	1.0	2.6	0	6.0
R	0.57	1.25	0	4.0	0.8	0.9	0	5.0	0.4	0.6	0	1.5
S	8.6	4.8	0	20.0	4.3	4.0	0	13.0	4.3	0.9	0	8.0
T	−0.36	1.42	−3.0	+5.0	−2.31	0.92	−5.0	+1.5	−2.2	0.67	−3.0	+1.0
aV_F												
Q	0.24	0.53	0	4.0	0.5	1.4	0	3.0	0.4	1.0	0	5.0
R	4.7	4.0	0	21.0	1.3	8.3	0	20.0	2.7	2.2	0	8.0
S	2.3	2.9	0	10.0	0.2	1.3	0	8.0	1.6	1.4	0	4.0
T	0.52	1.46	−4.0	+10.0	1.86	1.1	−0.5	+5.0	1.4	0.92	−0.5	+3.0

*ID = time of onset of intrinsic deflection from the beginning of the QRS complex.

ventricle (such as hypertension, aortic valvular lesions, coarctation of the aorta, patent ductus arteriosus) was present. Fifty-three patients were excluded from this study because they had received digitalis or quinidine, had angina pectoris or known coronary disease, or because their electrocardiograms exhibited bundle branch block or Q waves consistent with the possibility of myocardial infarction. One hundred forty-seven patients remained of whom 90 per cent had hypertension exceeding 155/95, with a mean blood pressure of 197/117, and a mean increase in the transverse diameter of the heart[20] of 15.8 per cent. Electrocardiographic studies of the patients in this group were made as will be described in detail later. As controls, 151 normal subjects, whose histories, physical examinations, electrocardiograms, and roentgenograms of the chest gave negative results, were studied similarly. This control group consisted of healthy nurses, medical students, members of the house staff, and flying personnel of a commercial airline. The mean age of the normal subjects was 35.1 years.

The standard limb leads were obtained first in each case. The augmented unipolar limb leads (aV_L, left arm; aV_R, right arm; and aV_F, left leg) and the unipolar precordial leads (V_1 through V_6) were then obtained by the method of Goldberger[17] in his modification of Wilson's central terminal. In addition, seven-foot chest films were taken in all but fourteen cases.

The electrocardiographic abnormalities considered to be particularly significant included the criteria previously noted in the literature,[5-11,18,19] as well as the variations in the unipolar leads to be described.

The electrocardiograms were analyzed in tabular form on master sheets, all waves of each record being carefully measured (with a magnifying lens if necessary). The amplitude of upright waves was measured from the upper edge of the base line to the peak of the wave; that of inverted waves, from the lower edge. Calibration corrections were applied, if necessary, for standardization (1.0 cm. = 1.0 mv.). Particular attention was paid to the voltage of the R and S waves in the precordial and unipolar extremity leads in order to calculate the ratios to be described. Gubner and Ungerleider[10] have emphasized the diagnostic importance of high voltage of the QRS complex in the standard limb leads in left ventricular hypertrophy. The data to be presented will aid in establishing the importance of high voltage in the precordial and extremity leads which had not been evaluated by the authors just mentioned. In addition, data on the total left ventricular potentials (the sum of the amplitudes of the R wave in Lead V_5 and the S wave in Lead V_1) of normal subjects were compared with those of patients with left ventricular hypertrophy.

RESULTS

Table I summarizes the statistical data obtained in the cases of left ventricular hypertrophy, in the entire normal group as well as in the subjects with left axis deviation included in the normal group. Table II summarizes the criteria obtained from a study of our data for the diagnosis of left ventricular hypertrophy when the changes occur in the presence of hypertension or a cardiac lesion putting strain on the left ventricle. Table III summarizes the frequency with which the various electrocardiographic abnormalities were encountered.

TABLE II. THE CRITERIA FOR THE DIAGNOSIS OF LEFT VENTRICULAR HYPERTROPHY

1. Standard limb leads
   (a) Voltage $R_1 + S_3 = 25$ mm. or more.
   (b) RS-T_1 depressed 0.5 mm. or more.
   (c) T_1 flat, diphasic, or inverted, particularly when associated with (b) and a prominent R wave.
   (d) T_2 and T_3 diphasic or inverted in the presence of tall R waves and (b).
   (e) T_3 greater than T_1 in the presence of left axis deviation and high voltage QRS complex in Leads I and III.
2. Precordial leads
   (a) Voltage of R wave in V_5 or V_6 exceeds 26 millimeters.
   (b) RS-T segment depressed more than 0.5 mm. in V_4, V_5, or V_6.
   (c) A flat, diphasic, or inverted T wave in Leads V_4 through V_6 with normal R and small S waves and (b).
   (d) Ventricular activation time in V_5 or $V_6 = 0.06$ second or more, especially when associated with a tall R wave.
3. Unipolar limb leads
   (a) RS-T segment depressed more than 0.5 mm. in aV_L or aV_F.
   (b) Flat, diphasic, or inverted T wave, with an R wave of 6.0 mm. or more in aV_L or aV_F and (a).
   (c) Voltage of R wave in aV_L exceeds 11.0 millimeters.
   (d) Upright T wave in aV_R.

TABLE III. THE FREQUENCY OF ABNORMALITIES IN UNIPOLAR LIMB AND PRECORDIAL LEADS IN LEFT VENTRICULAR HYPERTROPHY

Total number of cases		147
Total number of cases with normal or borderline standard leads		34
Abnormal RST-T findings		136
Lead I	69	
Lead II and/or III	20	
Leads V_4 through V_6	111	
Lead aV_L	88	
Lead aV_R	38	
Lead aV_F	40	
Abnormal voltage		67
$R_1 + S_3 = 25$ mm. or more	26	
R in V_5 or R in $V_6 = 26$ mm. or more	29	
R in $V_L = 11$ mm. or more	33	
R in V_5 + S in $V_1 = 35$ mm. or more	48	
Delayed onset of the intrinsic deflection (delayed ventricular activation time) 0.06 second or more in V_5 or V_6.		52

The cases of left ventricular hypertrophy were divided into three groups, depending on the size of the heart as determined by the method of Ungerleider and Clark.[20,21] In the group whose cardiac size fell within the normal range ($\pm$ 10 per cent of the expected), it was found in some that the contour of the left border of the heart suggested left ventricular hypertrophy. For purposes of

uniformity these cases were classified in the group with no cardiac enlargement. No definite association was observed between cardiac size and electrocardiographic abnormalities. In many instances, significant electrocardiographic findings were noted in the absence of cardiac enlargement. The reverse was seen less frequently.

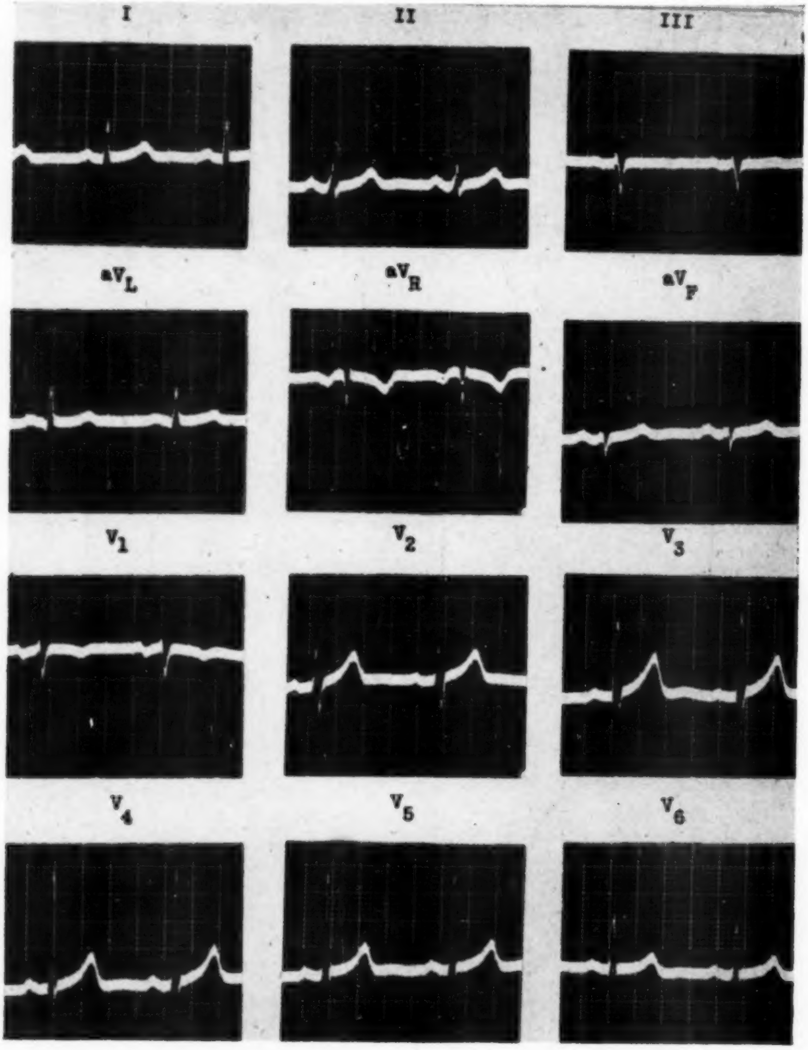

Fig. 1.—H. H., a 58-year-old man, U78776. Normal subject with horizontal position of the heart and left axis deviation (– 20°).

Position of the Heart.—The electrocardiographic position of the heart was determined in each case (Table IV). It will be seen that the majority of the patients had horizontal or semihorizontal hearts. Because of the horizontal position of the heart, left axis deviation was present. It will be shown later that

the electrocardiographic patterns of patients with horizontal hearts are those described in the literature as typical of left ventricular hypertrophy.[6,9] Some of the cases classified as intermediate in position may in fact have been semi-horizontal because the major abnormalities in these cases were seen in Lead aV_L. Although the R wave was significantly upright in both Leads aV_L and aV_F, the contribution of the left ventricle was often seen to a greater degree in the changes in the left arm lead.

An attempt was made to differentiate the electrocardiographic findings in normal horizontal hearts with left axis deviation from the electrocardiographic abnormalities found in hearts with left ventricular hypertrophy and left axis deviation. Table I reveals that the findings in the electrocardiograms of normal subjects with left axis deviation do not differ significantly from the findings in the entire normal control group. No RST-T abnormalities or abnormal voltage of the R or S waves occurred in the standard, unipolar limb, and precordial leads in normal horizontal hearts (Fig. 1), although it is perhaps possible theoretically for very marked counterclockwise rotation to cause an inverted T wave in aV_L.[29] Furthermore, the time of onset of the intrinsic deflection was not found to be greater than 0.05 second in the normal individual.

TABLE IV. THE ELECTROCARDIOGRAPHIC POSITION OF THE HEART AS OBTAINED IN 147 CASES OF LEFT VENTRICULAR HYPERTROPHY

Horizontal	31
Semihorizontal	52
Intermediate	30
Semivertical	26
Vertical	6
Indeterminate	2
	147

The RST-T Pattern of Left Ventricular Hypertrophy in Horizontal Hearts.—The importance of abnormalities of the RS-T segment and T wave in the recognition of left ventricular hypertrophy is clearly seen from Table III, these changes being the most frequent of all the abnormal findings.

The patterns of left ventricular hypertrophy seen in horizontal and semi-horizontal hearts (Figs. 2 through 5) show the "typical" changes in the standard leads because the position of the heart is horizontal. The left ventricular potentials (V_5 and V_6) are directed toward the left arm (aV_L) which in turn result in changes in Lead I. Hence, the typical RST-T variations of left ventricular hypertrophy in horizontal hearts may be seen in Leads I, aV_L, and V_4 through V_6. The precordial leads were usually the first to become abnormal, but occasionally the left arm lead revealed flat or inverted T waves when the RST-T changes in the precordial leads were borderline (Fig. 4).[10,11] This was true even though precordial leads were taken in the seven positions in both the third and fifth intercostal spaces. The abnormalities seen in Lead aV_L were usually more marked than those noted in Lead I but, as a rule, were less striking than those found in Leads V_5 and V_6.

Depending on the stage of evolution of the electrocardiographic pattern, the RST-T changes were minimal (Lead I in Fig. 3), moderate (Lead aV_L in Fig. 2), or marked (Lead V_5 in Fig. 5). In the well-developed pattern, the typical RST-T relationship, as previously emphasized by Rykert and Hepburn[5]

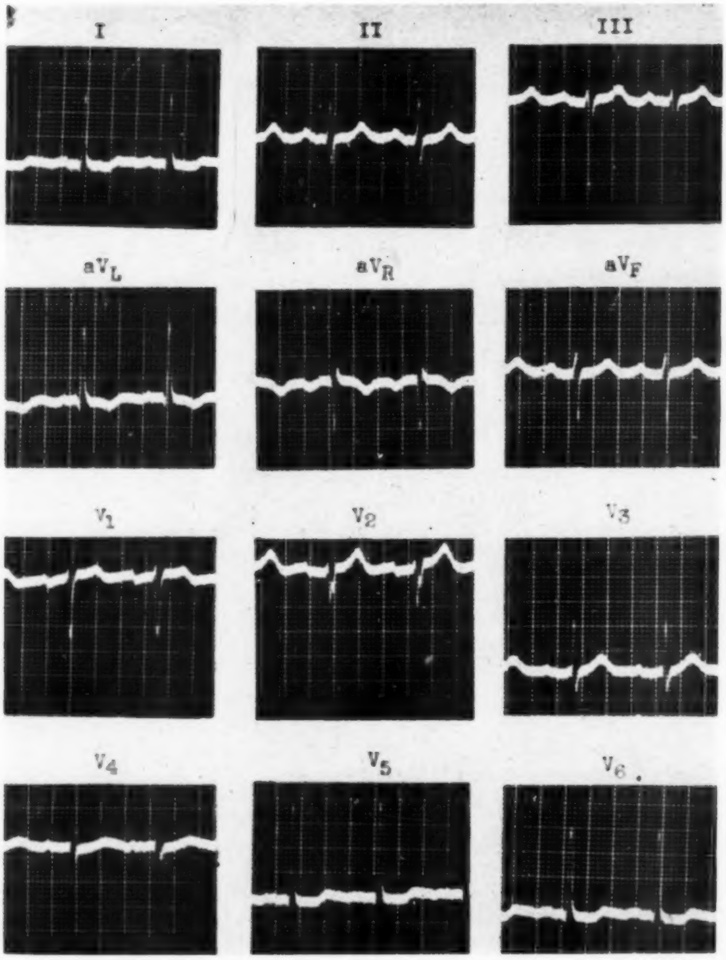

Fig. 2.—E. G., a 72-year-old woman, U132714. Hypertension. Left ventricular hypertrophy in a horizontal heart. Note the RST-T abnormalities in Leads I, aV_L, V_5, and V_6. In addition, the intrinsic deflection occurs in 0.06 second in V_6, the voltage of the R wave in aV_L equals 14 mm., and $R_1 + S_3$ equals 28 mm.

and by Kaplan and Katz,[9] was clearly seen in the left precordial leads and, depending on the position of the heart, these same abnormalities appeared in the left arm or the left leg lead. This contour was significant and was characterized in its typical form by an RS-T segment that was depressed and bowed upward and by a T wave that was inverted and asymmetric (V_5 in Fig. 5). The RS-T segment and T wave were both directed downward, in contrast to the usual appearance in coronary disease where the RS-T and T are in opposite directions

if the RS-T segment is elevated or depressed. In the early developing stages of left ventricular hypertrophy, the RST-T relationship was less clear. Often the T wave decreased in size before the changes in the RS-T segment appeared or slight depression of the RS-T segment was associated with a lowered T wave;

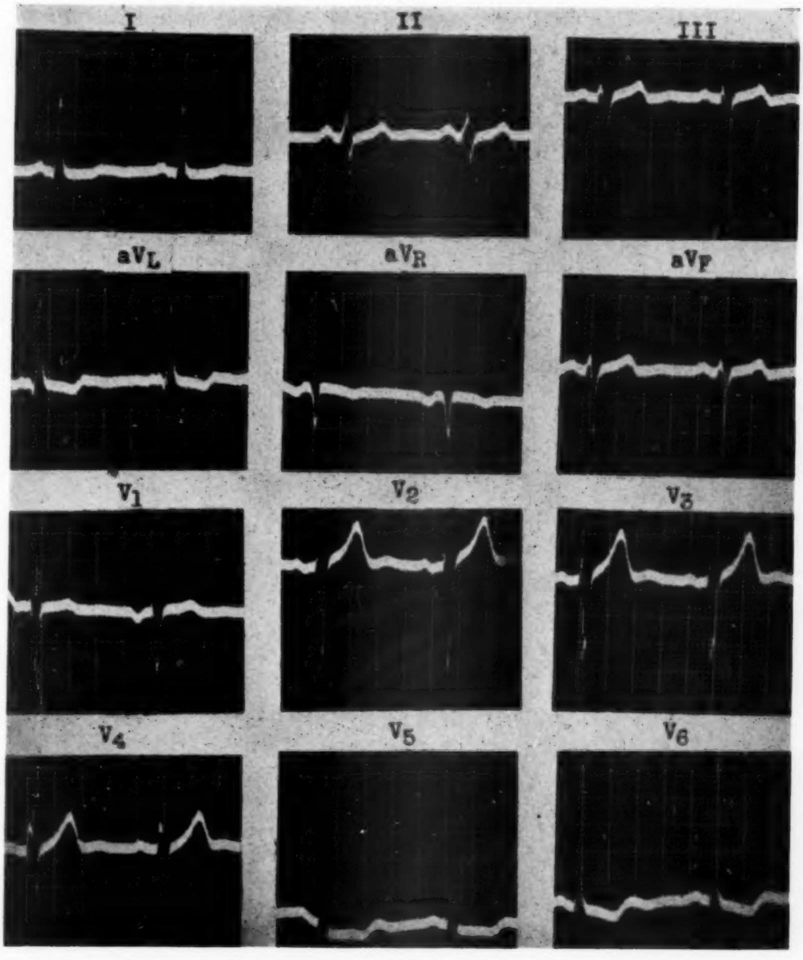

Fig. 3.—I. R., a 69-year-old man, U133478. Hypertension. Left ventricular hypertrophy in a horizontal heart. Note the characteristically abnormal RST-T contour in V_6 and aV_L with the early RST-T contour in Lead I. The voltage of $R_1 + S_3$, of R in aV_L, and of R in V_5 + S in V_1 are also abnormal.

in these cases the RS-T segment and T wave were not always in the same direction early in the disease (Lead I in Figs. 2 and 3). Some patients have the characteristic RST-T relationship of left ventricular hypertrophy in one lead (V_6 in Fig. 3) with the early relationship in another (Lead I in Fig. 3).

Low T waves were frequently observed in the left precordial leads in the patients with left ventricular hypertrophy, although no record was classified as abnormal on the basis of low T waves. To quantitate this finding, the ratio

of the amplitude of R to T was calculated in all the patients with upright T waves (those with flat, diphasic, or inverted T waves were excluded). Table IX summarizes the data obtained. The results were significant in that the ***mean*** R/T ratio in Leads V_5 and V_6 in the cases of left ventricular hypertrophy exceeded the *maximum* R/T ratio in these leads found in normal subjects. Fifty per cent of the patients with left ventricular hypertrophy with upright T waves

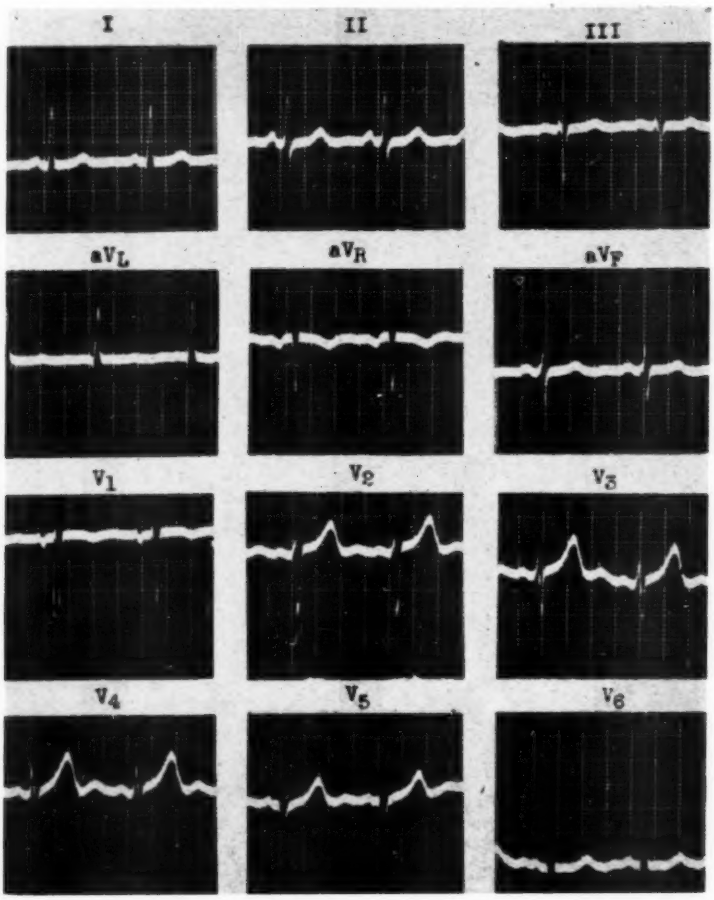

Fig. 4.—A. D., a 36-year-old woman. Hypertension of eight years' duration. Cardiac enlargement +25 per cent. Standard leads normal except that the ratio T_3/T_1 is 1 in presence of left axis deviation. A flat T wave in aV_L with an R wave of 9 mm. is the only abnormality except that the combined voltage of R in V_6 and S in V_1 is 44 millimeters. This record represents the earliest findings in left ventricular hypertrophy in a semihorizontal heart.

in V_5 and/or V_6 had an R/T ratio in these leads equalling or exceeding the maximum normal ratio of 10. It was of interest to note that the R wave was absent in Lead V_3 in only six of the 147 patients with left ventricular hypertrophy and in none in Leads V_4, V_5, or V_6.

The RST-T Pattern of Left Ventricular Hypertrophy in Electrocardiographically Vertical Hearts.—The electrocardiographic patterns of left ventricular hyper-

trophy in a vertical or semivertical heart (Figs. 6 and 7) illustrate that individuals with this type of hypertrophy do not have the changes in axis or in RST-T that have long been considered "typical" in the standard limb leads.[4-10] When the heart is electrocardiographically vertical the potential changes of the left ventricle are directed toward the left leg so that Leads II, III, and aV_F, but not Lead I, reveal the RST-T abnormalities originating in the left ventricle. Furthermore, the electrical axis may be directed toward the right. The precordial Leads V_5

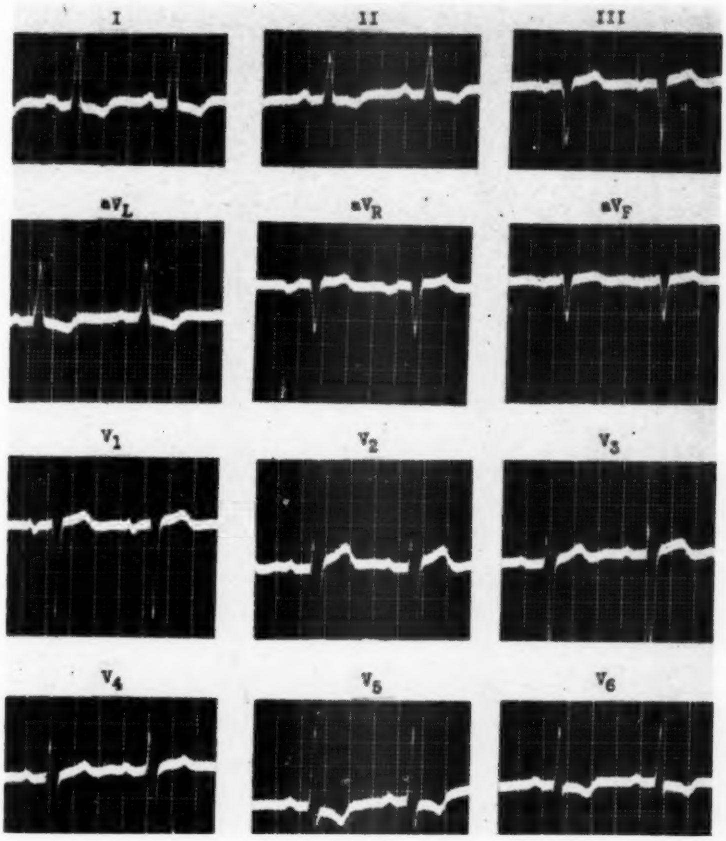

Fig. 5.—C. B., a 62-year-old woman. Hypertension. Typical left ventricular hypertrophy in a horizontal heart with the classic RST-T contour in Leads I, II, aV_L, V_5, and V_6. Note the upright T wave in aV_R. The voltage of $R_1 + S_3$ and of the R wave in aV_L is just beyond the critical level. The onset of the intrinsic deflection is not delayed.

and V_6 show the same type of abnormalities in left ventricular hypertrophy, whether the heart is vertically or horizontally placed (Figs. 2 through 9). Variations in the standard leads in these cases merely reflect the electrocardiographic position of the heart, and the position determines whether the potential changes of V_5 and V_6 (representing the left ventricle) are transmitted to the left leg (and hence to Leads II and III), or to the left arm (and hence to Lead I).

Lead aV_F was at times of definite diagnostic value when left ventricular hypertrophy occurred in a vertical heart, as illustrated in Fig. 8. In this particular case the changes in Leads II and III were not diagnostic and the only abnormalities in V_5 and V_6 were slight depression of the RS-T segment. Possibly Leads V_7 or V_8 would have shown greater abnormalities if the transitional zone had been displaced farther to the left. Nevertheless, with the usual records, the significant abnormalities were seen mainly in Lead aV_F. This particular record

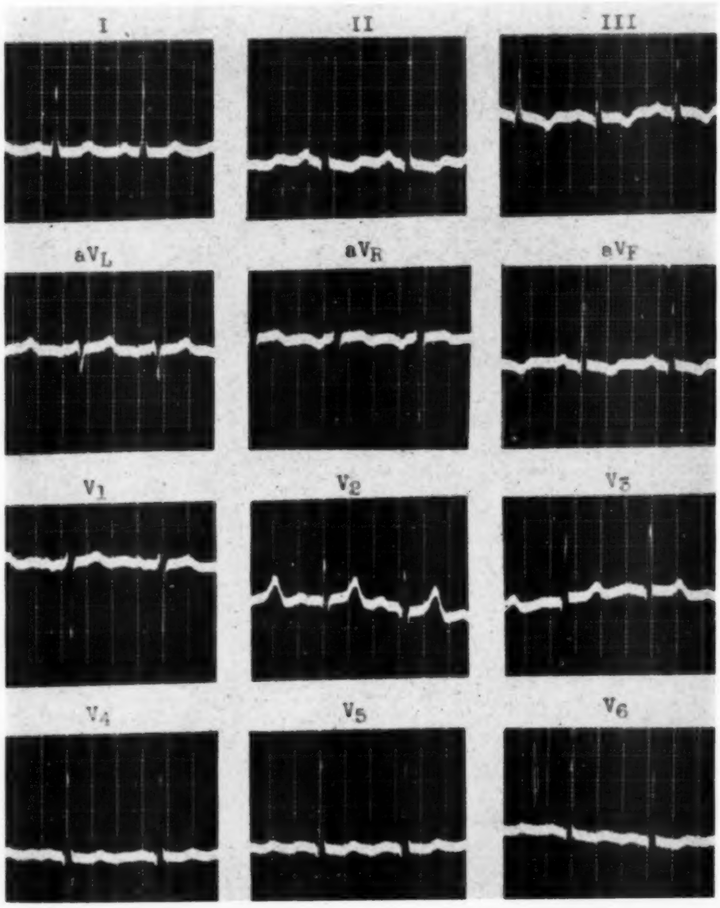

Fig. 6.—T. M., a 39-year-old woman, U136786. Hypertension. Left ventricular hypertrophy in a semivertical heart. Note the RST-T abnormalities in Leads II, III, and aV_F, and to a lesser extent, in V_4 through V_6.

was interpreted as representing left ventricular hypertrophy when the daily records were being routinely read; no history of the patient was available. When the patient was seen later, it was found he had hypertension.

Intrinsic Deflection.—Wilson and his associates[11] emphasized the importance of the time of appearance of the intrinsic deflection in the recognition of ventricular hypertrophy and bundle branch block. They stated that the time from the onset

of the QRS to the peak of the R wave or the beginning of the abrupt downstroke of the QRS represents the time interval required for the passage of the impulse through the ventricle to the epicardium underlying the exploring electrode. This time interval will be referred to in this paper as the "ventricular activation

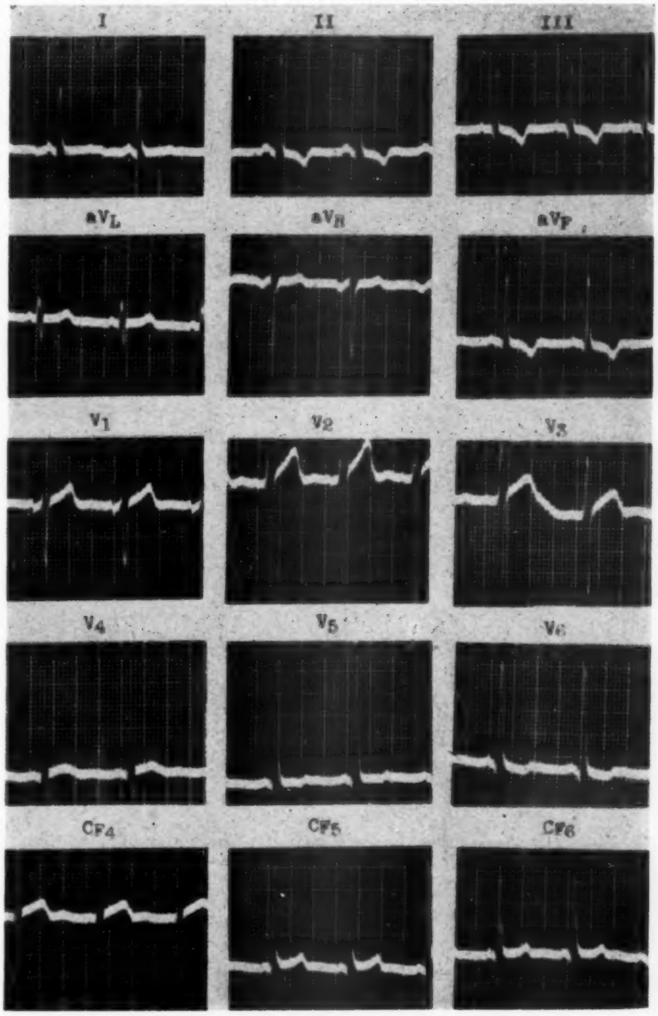

Fig. 7.—D. H., a 26-year-old man, U125144. Coarctation of the aorta. Cardiac enlargement, 20 per cent. Typical left ventricular hypertrophy in a vertical heart with abnormalities in Leads II, III, aV_F, V_5, and V_6.

time." An increased mass of myocardium, as present in left ventricular hypertrophy, would be expected to delay this time interval required for the passage of the impulse to the epicardium. In three different series of normal subjects, comprising 280 cases,[16,22,23] the onset of the intrinsic deflection (ventricular activation time) in Leads V_5 or V_6 was less than 0.06 second. Kossmann and

Johnston[22] stated that the time of onset of the intrinsic deflection in the normal individual averages 0.02 second in Lead V_1 and 0.04 second in V_5. Sodi-Pallares and his associates[16] in their study of 100 normal subjects found the maximum ventricular activation time in V_5 to be 0.05 second. In the present control series of normal subjects (Table I) 0.03 second in V_1 and 0.05 second in V_5 or V_6 was the upper limit of normal found.[23] Sixteen (10 per cent) of our normal subjects had a figure of 0.05 second in Leads V_5 or V_6.

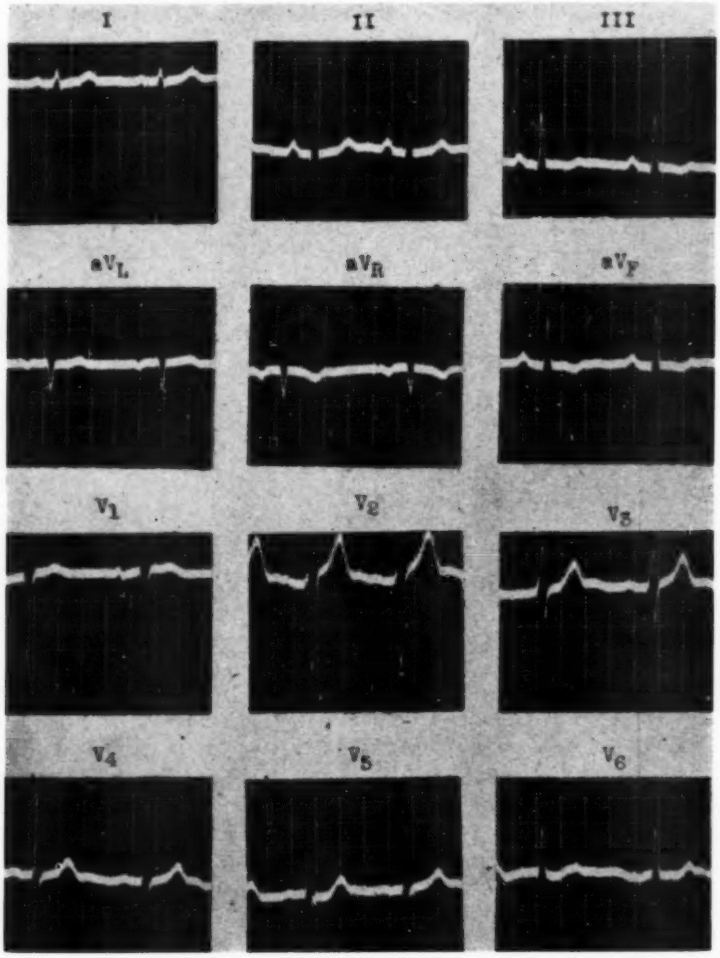

Fig. 8.—E. V. Y., a 29-year-old man. Hypertension. Left ventricular hypertrophy in a vertical heart. The major abnormality is present in Lead aV_F with minor RS-T segment depression in V_5 and V_6. The standard and unipolar precordial leads alone would not have been sufficient for a proper diagnosis.

In the present series of 147 cases of left ventricular hypertrophy, 85 (58 per cent) had a ventricular activation time* in V_5 or V_6 of 0.05 to 0.08 second.

*The term "ventricular activation time" refers to the time in seconds from the beginning of the QRS complex to the onset of the intrinsic deflection.

In fifty-two cases (35 per cent), the left ventricular activation time was 0.06 second or greater (but less than 0.08 second). The mean ventricular activation time in V_5 or V_6 was 0.05 second in contrast to 0.04 second in the normal group. In 40 per cent of the cases of left ventricular hypertrophy, the time of onset of the intrinsic deflection was normal even though other typical findings, such as a

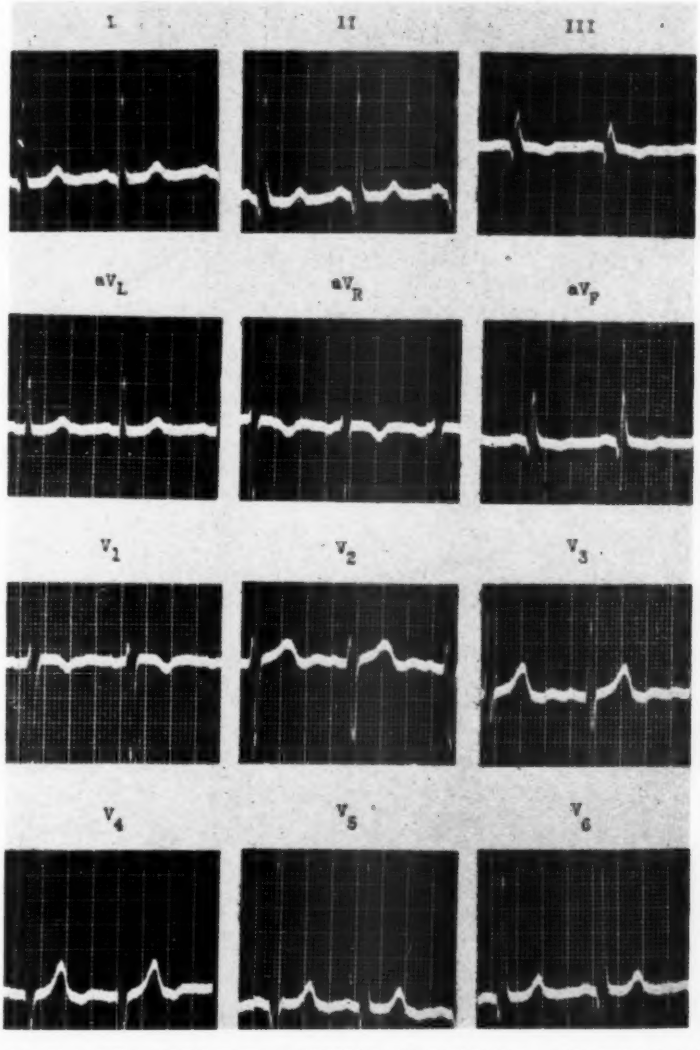

Fig. 9.—M. C., a 39-year-old woman, U128549. Hypertension. The voltage of R in V_5 and S in V_1 equals 49 millimeters. The ventricular activation time equals 0.06 second in V_5 and V_6. Early RST-T abnormalities are seen in Lead aV_F.

depressed R-ST segment and inverted T waves, were present (Fig. 5). In some patients, however, with long-standing hypertension and roentgenologic evidence of left ventricular enlargement, a delayed intrinsic deflection in Lead V_5 or V_6 was the only abnormal electrocardiographic sign. Is one justified in diagnosing

left ventricular hypertrophy solely by the presence of an intrinsic deflection that is delayed in V_5 or V_6? No normal individual in the three available series (total of 280 cases)[16,22,23] had a ventricular activation time of as much as 0.06 second. The majority of patients with left bundle branch block (Wilson's criteria[11]) had a ventricular activation time between 0.08 and 0.14 second; none was found to be shorter.[26] In contrast, approximately 50 per cent in Sodi-Pallares' series[16] and fifty-two of 147 (35 per cent) in the present series of left ventricular hypertrophy had a ventricular activation time of 0.06 second or longer. It must be concluded that such a finding, even as an isolated abnormality, should weigh heavily in favor of a diagnosis of left ventricular hypertrophy, especially if, in addition to a delayed intrinsic deflection, the R wave is tall and the T wave is relatively low in the same lead.

It was considered of interest to note the association between size of the heart (as obtained from the transverse diameter of the heart and the table of Ungerleider and Clark[20]) and the ventricular activation time. Thirteen (25 per cent) of the fifty-two patients in the series of 147 who had a ventricular activation time of 0.06 second had no cardiac enlargement. Of the ninety-five persons in whom this time interval was less than 0.06 second, thirty (31 per cent) had no cardiac enlargement. Thus, no association between a delayed intrinsic deflection and transverse cardiac diameter could be demonstrated. Cardiac hypertrophy may be present, however, without roentgenologic evidence of cardiac enlargement.

Intraventricular Conduction.—The relationship between the ventricular activation time and the total QRS duration was studied. It has been previously shown that in left ventricular hypertrophy the total QRS duration may exceed 0.10 second, often being 0.12 second without the electrocardiographic pattern of left bundle branch block being present.[11] This was confirmed by a study of the patients in this series in whom the QRS duration was 0.11 or 0.12 second. This duration was present in eighteen (12 per cent) of the 147 cases under discussion. In typical left bundle branch block, the left ventricular activation time almost always exceeded 0.08 second, whereas it very rarely reached this figure in left ventricular hypertrophy. Furthermore, in left ventricular hypertrophy with a QRS duration of 0.12 second and a delayed intrinsic deflection of 0.06 or 0.07 second, the peak of R in the ventricular complex usually was found to be tall and sharp. In left bundle branch block, the peak of R in Leads V_5 or V_6 is broad topped, notched, or "M" shaped, reflecting the delay in the spread of the impulse through the left ventricle. There was no constant relationship between the time of onset of the intrinsic deflection in Lead V_5 and the total QRS duration. Some patients had a normal activation time with a QRS of 0.12 second, while others had a delayed intrinsic deflection with a QRS of 0.10 second. The significance of these findings is not yet clear.

Voltage.—The importance of the voltage of the QRS complex was adequately demonstrated in the present series (Table III). In some cases the increased voltage was seen months or years before unequivocal RST-T changes occurred and as such was a valuable early diagnostic finding (Figs. 10 and 11).

The voltage of R and S in the unipolar leads can be seen in Table I. The mean height of the R wave in V_5 in left ventricular hypertrophy was 18.9 mm., and in normal subjects with horizontal hearts 11.8 mm. with a standard deviation of $\pm$ 5.4 millimeters. The maximum amplitude of R in V_5 in normal subjects was found to be 26 millimeters. This amplitude was exceeded in twenty-nine cases (20 per cent) of left ventricular hypertrophy. The amplitudes of the waves in the augmented unipolar extremity leads used in this study are 50 per cent greater than those obtained in the unipolar limb leads according to the

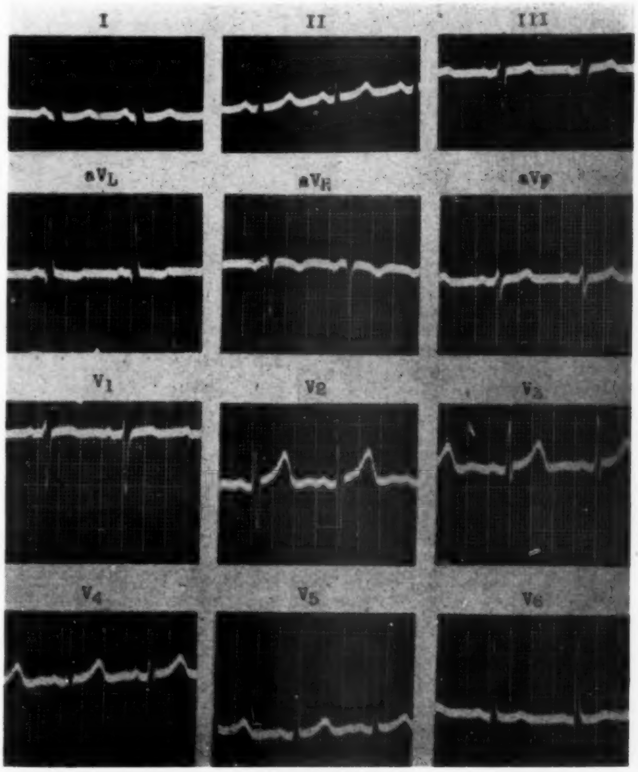

Fig. 10.—C. S., a 45-year-old woman, U86287. Hypertension. Sept. 6, 1946. The major abnormalities are seen in aV_L with high voltage of R (11.5 mm.) and early RST-T changes. The voltage of the R wave in Lead I is high, 16 millimeters.

method of Wilson. Also of value was the voltage of R in aV_L. The amplitude of this wave in normal horizontal hearts was found to be 4.6 mm. with a standard deviation of $\pm$ 2.5 mm., in contrast to the cases of left ventricular hypertrophy in which the corresponding figure was found to be 8.1 $\pm$ 4.8. In normal horizontal hearts, 99 per cent of the subjects may be expected to have an R wave in aV_L of less than 11.1 millimeters. In normal subjects the maximum R in aV_L was found to be 10.5 millimeters. This voltage was exceeded in thirty-three cases (22 per cent) of left ventricular hypertrophy. The diagnostic value of the

voltage of the R wave in Lead aV_F was less because the normal height of this wave is often great (up to 20 mm.).

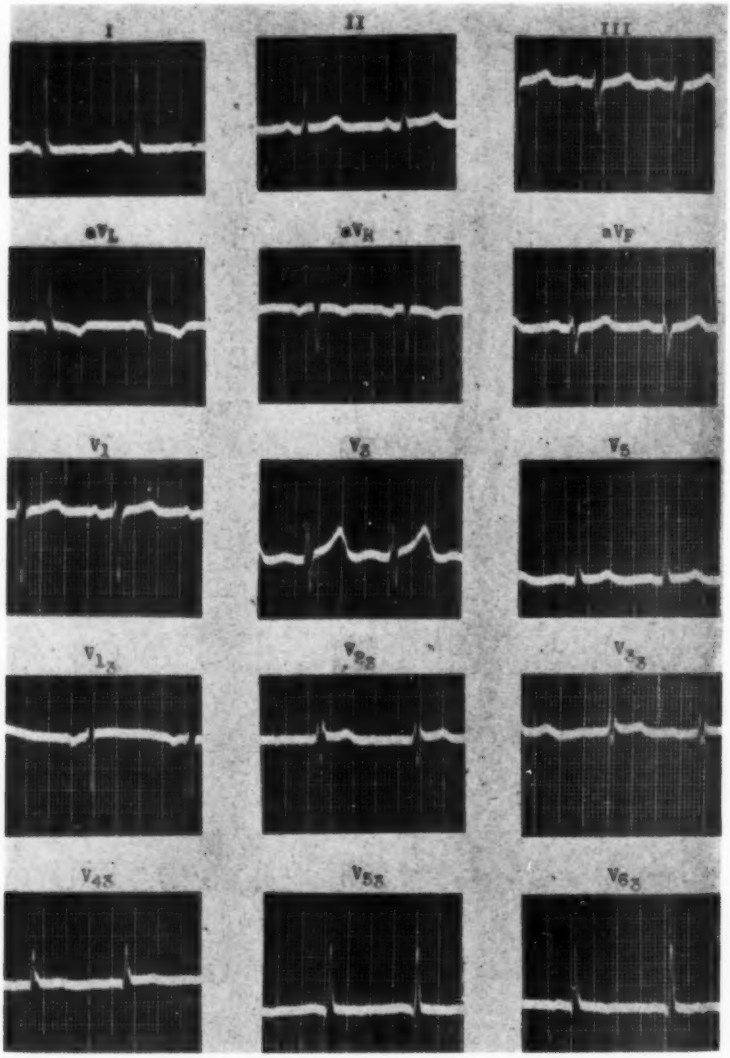

Fig. 11.—Same patient as in Fig. 10. June 6, 1947. Progressive abnormalities have appeared in aV_L and now Lead I and also Lead V_5 recorded in the third intercostal space are abnormal. Note that V_5 recorded in the third intercostal space is more abnormal than the conventional V_5 recorded in the fifth intercostal space.

In addition to the absolute value of the height of the R wave, the relationship of the R to the S wave in Leads V_1 and V_5 was found to be quite different in the group with left ventricular hypertrophy as compared with the normal individuals (Table V). The differences between the two groups were more strikingly evident when the ratio of $\frac{R/S \text{ in } V_5}{R/S \text{ in } V_1}$ was determined (Table VI). Of the

forty-two cases of left ventricular hypertrophy in which this ratio could be determined (indicating an R wave in V_1 and an S wave in V_5), fourteen cases (33 per cent) exceeded the maximum normal ratio of 100.

TABLE V. THE R/S RATIO IN THE UNIPOLAR PRECORDIAL LEADS OF CASES OF LEFT VENTRICULAR HYPERTROPHY AS COMPARED WITH NORMAL SUBJECTS

	NORMAL			LEFT VENTRICULAR HYPERTROPHY		
	MEAN	ST. DEV.	RANGE	MEAN	ST. DEV.	RANGE
R/S ratio						
V_1	0.3	0.3	(0-1.0)	0.08	0.11	(0-0.6)
V_2	0.2	1.2	(0.1-13)	0.65	2.05	(0-20)
V_3	1.4	1.4	(0.1-10)	2.6	6.1	(0-56)
V_4	4.1	3.8	(0.2-19)	5.8	6.6	(0.2-38)
V_5	7.3	4.7	(1.0-24)	10.7	9.2	(1.6-50)
V_6	9.0	5.0	(2.3-22)	15.7	11.2	(4.2-38)

TABLE VI. THE RESULTS OF THE R/S RATIO IN V_5 DIVIDED BY THE R/S RATIO IN V_1 IN NORMAL SUBJECTS AND THOSE WITH LEFT VENTRICULAR HYPERTROPHY

	NORMAL	LEFT VENTRICULAR HYPERTROPHY
$\frac{\text{R/S in } V_5}{\text{R/S in } V_1}$		
Mean	32.0	98
Standard deviation	26.9	91.5
Range	3.1–100	13–400

The sum of the total left ventricular potentials (S wave in V_1 plus R wave in V_5 or R wave in V_6) proved to be of definite diagnostic importance (Table VII). The mean sum in the normal subjects was 19.9 ± 5.6 mm.; in only six (4 per cent) of 150 normal individuals did the sum exceed 30 and none exceeded 35 millimeters. This is in contrast to the findings obtained in the 147 patients with left ventricular hypertrophy in seventy-two (49 per cent) of whom the sum of the S wave in V_1 and the R wave in V_5 or V_6 exceeded 30 mm. and in forty-eight (32 per cent) of whom this sum exceeded 35 millimeters. In approximately one-third, therefore, of the cases of left ventricular hypertrophy the sum of R in V_5 and

TABLE VII. THE SUM OF THE AMPLITUDES (IN MILLIMETERS) OF THE R WAVE IN V_5 AND THE S WAVE IN V_1 IN NORMAL SUBJECTS AND SUBJECTS WITH LEFT VENTRICULAR HYPERTROPHY

R IN V_5 + S IN V_1	NORMAL	LEFT VENTRICULAR HYPERTROPHY
Mean	19.9	30
Standard deviation	± 5.6	± 10.4
Range	0–35	12–65

S in V_1 exceeded the maximum sum obtained in normal subjects. In some cases, abnormal voltage of R in V_5 or V_6 and S in V_1 and minor T-wave changes were the only abnormalities (Fig. 4). Re-evaluation of some of the electrocardiograms of patients with hypertension not included in the present study because the records were interpreted as normal revealed a number that would have been classified as abnormal if the data on voltage here presented had been used. The single measurement of the sum of the R waves in V_5 or V_6 (whichever is larger) and the S wave in V_1 is an apparently reliable criterion of left ventricular hypertrophy (Table III).*

The variety of data on abnormally high voltage proved helpful because the high voltage was seen in different combinations in different cases. Fig. 2 illustrates high voltage of the R wave in aV_L (14 mm.) and high voltage in the sum of $R_1 + S_3$ (31 mm.); the sum of S in V_1 and R in V_5 is within normal limits (31 mm.). In Fig. 4 the voltage of $R_1 + S_3$ (21 mm.) and of R in aV_L (10 mm.) is within the normal range, yet S in V_1 + R in V_6 is definitely abnormal (45 mm.). In Fig. 3 all three measurements of voltage are high.

Q Waves.—The evaluation of the Q waves in the unipolar precordial and limb leads is no less difficult than in the standard limb leads. The criteria suggested for abnormality of the Q waves vary widely.[24,25,26] A Q wave may normally be found in the left precordial leads and in any unipolar lead taken from a point on the body toward which the left ventricular potentials are directed. Thus, in horizontal hearts, a Q wave may normally be seen in aV_L as well as in Leads V_4 through V_6; in vertical hearts, Q waves can be found in aV_F and in Leads V_4 through V_6. Q waves were commonly seen in our cases of left ventricular hypertrophy, being found in approximately one-third of the cases in the left precordial leads and in Lead aV_L (Table VIII). Rarely did the Q waves exceed

TABLE VIII. THE Q/R RATIO IN PATIENTS WITH LEFT VENTRICULAR HYPERTROPHY AS COMPARED WITH SUBJECTS WITH NORMAL HEARTS

LEAD	NORMAL					LEFT VENTRICULAR HYPERTROPHY				
	NO.	MEAN	ST. DEV.	MIN.	MAX.	NO.	MEAN	ST. DEV.	MIN.	MAX.
V_1	0	0	0	0		0	0	0	0	
V_2	0	0	0	0		4	0.06	0.05	(0	0.13)
V_3	2	0.025	0.002	(0	0.03)	5	0.072	0.059	(0	0.14)
V_4	16	0.04	0.032	(0	0.1)	21	0.043	0.002	(0	0.1)
V_5	49	0.07	0.039	(0	0.16)	48	0.055	0.038	(0	0.23)
V_6	65	0.087	0.043	(0	0.21)	51	0.072	0.045	(0	0.25)
aV_L	20	0.238	0.165	(0	0.75)	43	0.147	0.178	(0	1.0)
aV_R	43	4.97	2.96	(0	14.0)	17	6.02	4.75	(0	20.0)
aV_F	58	0.1	0.06	(0	0.28)	38	0.15	0.14	(0	0.77)

*A recent patient followed to autopsy illustrates the diagnostic value of the voltage of the precordial leads. A 16-year-old boy with coarctation of the aorta had a normal-sized heart by x-ray study. The electrocardiogram was entirely normal except that the sum of the R wave in V_5 and the S wave in V_2 equalled 50 millimeters. The S wave in V_2 was 36 millimeters (the maximum obtained in our normal subjects was 29 mm.). At autopsy the left ventricular wall measured 2.0 cm. in thickness. There was no coronary disease or myocardial fibrosis. The heart weighed 300 grams.

3.0 mm. in depth in left ventricular hypertrophy, and when the Q waves were of that depth, the R waves in the corresponding lead were tall. The maximum Q/R ratio in the left precordial leads in left ventricular hypertrophy was found to be 25 per cent (Table VIII).

The interpretation of Q waves, especially in Lead aV_L in semivertical hearts, is extremely difficult. When the Q is wide (0.04 second), when it represents 50 per cent of the QRS complex, and when it is followed by a convex elevated RS-T segment and a late inversion of T, a lateral myocardial infarction should be suspected.[27] Unipolar leads made in the second and third intercostal spaces should be taken if the routine precordial leads are not diagnostic in order to recognize a high anterior lesion. However, in some cases, no further electrocardiographic support for myocardial infarction can be elicited by exploratory precordial leads. In the normal subjects of our series in whom Q waves in aV_L represented 50 per cent of the R wave, the total QRS complex was small (less than 5.0 mm.).

TABLE IX. THE RATIO OF THE AMPLITUDES OF THE R AND T WAVES (R/T RATIO) IN PATIENTS WITH LEFT VENTRICULAR HYPERTROPHY AS COMPARED WITH SUBJECTS WITH NORMAL HEARTS. THE RATIO IS CALCULATED ONLY WHEN THE T WAVE IS UPRIGHT; FLAT, DIPHASIC, OR INVERTED T WAVES ARE EXCLUDED

LEAD	NORMAL (151 CASES)				LEFT VENTRICULAR HYPERTROPHY (147 CASES)			
	NO.	MEAN	ST. DEV.	RANGE	NO.	MEAN	ST. DEV.	RANGE
V_1	59	1.4	0.9	(0.3–7)	68	1.0	1.0	(0.1–4)
V_2	145	1.4	1.4	(0.2–12)	123	1.3	1.4	(0.1–7)
V_3	150	1.9	1.6	(0.3–13)	114	3.0	3.2	(0.1–20)
V_4	150	3.1	2.3	(0.3–9)	99	6.1	3.9	(0.6–23)
V_5	151	3.5	1.6	(1.0–9)	68	10.9	7.4	(2.7–44)
V_6	151	4.1	1.9	(1.7–10)	60	11.1	6.6	(2.7–34)
V_L	91	2.6	1.9	(0.1–10)	40	8.1	7.4	(0.3–28)
V_F	142	4.6	3.2	(0.3–14)	81	4.4	4.5	(0.3–28)
V_R		0	0	0		0	0	0

ASSOCIATED CORONARY DISEASE AND MYOCARDIAL INFARCTION

Coronary arteriosclerosis is commonly found at autopsy in patients with hypertension and left ventricular hypertrophy. It is not surprising, therefore, that changes typical of myocardial infarction or coronary insufficiency frequently coexist with signs of left ventricular hypertrophy. The factors of left ventricular hypertrophy and coronary insufficiency cannot be adequately separated when the RS-T contour and T-wave changes are characteristic of coronary insufficiency.[8] Probably myocardial infarction can be diagnosed in conjunction with left ventricular hypertrophy when the Q, RS-T segment, and T-wave changes typical of myocardial infarction are present concurrently with signs of left ventricular hypertrophy, such as high voltage and typical RST-T changes. One of the major values of unipolar precordial and limb leads is their ability to

uncover an unsuspected myocardial infarction (usually anteroseptal and old) when the standard limb leads are either normal or the abnormalities are nonspecific. Many instances of myocardial infarction are clinically occult, and unipolar studies in patients in whom myocardial infarction is common (for example, patients with hypertension) will allow unsuspected myocardial infarction to be recognized occasionally. Despite the fact that myocardial infarction clinically may not be typical, it is rarely completely silent. In a recent study of thirty patients with hypertension in whom a previously unsuspected diagnosis of myocardial infarction was made from the unipolar leads, practically all had some episode in the past history compatible with the diagnosis.[27] Sudden weakness, sunstroke, sudden cardiac failure, hemiplegia, pulmonary embolism, and sudden paroxysmal nocturnal dyspnea were frequently noted in the relatively recent past history of these patients. Therefore, unipolar leads are valuable not only in delineating the characteristic features of left ventricular hypertrophy, but in excluding or establishing the presence of associated coronary insufficiency or myocardial infarction.

DISCUSSION

The electrocardiographic diagnosis of left ventricular hypertrophy depends upon proper evaluation of two particular problems in so far as the standard limb leads are concerned: (1) the differentiation of "normal" from "abnormal" left axis deviation; (2) the interpretation of RST-T changes (especially in Leads II and III) in the absence of left axis deviation and in the absence of abnormal RST-T changes in Lead I. As far as the first problem is concerned, the diagnosis is fairly simple when the typical RST-T changes of left ventricular hypertrophy occur in association with high voltage QRS waves and left axis deviation. When the RS-T segment and T wave in Lead I are essentially normal and the voltage of R_1 and S_3 is not abnormal, the problem is more difficult. It is then necessary to study the precordial and unipolar extremity leads in order to differentiate transverse position of the heart or counterclockwise rotation of the heart on its longitudinal axis[28] from left ventricular hypertrophy. Left axis deviation and the associated transverse position of the heart in young people should immediately arouse suspicion of abnormality, especially if the individual is of average build. Horizontal or semihorizontal hearts with left axis deviation were infrequently found in normal subjects under the age of 40 years in the absence of obesity or conditions, such as pregnancy, that elevate the diaphragm.[23] Many persons who were overweight did not have horizontal hearts as might be expected.[23] In older and stout individuals, left axis deviation and transverse hearts were more commonly seen without left ventricular hypertrophy, and additional substantiation was required from the precordial and unipolar limb leads in order to establish a diagnosis. These leads were of particular value because it was not uncommon for typically abnormal RST-T signs to be found in Leads V_5 or V_6 or aV_L when they were absent or not characteristic in Lead I (Fig. 3). At times, because of unknown factors, possibly rotation, the abnormal left ventricular potentials may be transmitted to the left arm, and Lead aV_L

may be more abnormal than V_5 or V_6 (Figs. 10 and 11); this, however, was unusual. Because Lead I reflects the difference in potential between the left and right arms, an abnormal T wave in the left arm may be neutralized by the potential of the right arm, and hence Lead I may be normal and Lead aV_L abnormal. The deviation of the T wave to the right, with T_3 becoming equal to or greater than T_1 in the presence of a horizontal or semihorizontal heart, reflects the abnormality of the T wave in aV_L. Such progressive "rightward deviation" of the T wave in the standard leads occurs coincidentally with progressive lowering of the T wave in aV_L in cases of hypertension with horizontal hearts (Figs. 10 and 11) and we have found the observations of Proger and Minnich[18] and of Ashman and Hidden[19] to be of value. Even when both Lead I and Lead aV_L are abnormal, the degree of abnormality is usually greater in the left arm lead (Fig. 11). Therefore, the unipolar left arm lead (aV_L), as well as the unipolar precordial leads (especially V_5 and V_6), are very helpful in evaluating the significance of left axis deviation in the standard leads in the presence of normal RS-T segments and T waves.

In the interpretation of RST-T changes in the standard leads in the absence of left axis deviation, or in the presence of right axis deviation, unipolar precordial and extremity leads are even more valuable (Fig. 7). As already noted, the typical pattern of left ventricular hypertrophy with left axis deviation and abnormal RST-T in Lead I occurs in individuals with horizontal hearts (Fig. 5). Because of the transmission of the left ventricular potential to the left leg in persons with vertical hearts, the characteristic RST-T changes of left ventricular hypertrophy will occur in the left leg lead and in standard Leads II and III (Fig. 7). The precordial leads, however, in left ventricular hypertrophy in vertical hearts are similar to those obtained in left ventricular hypertrophy in horizontal hearts. The dissimilarity in the standard leads in vertical and horizontal hearts (the absence of left axis deviation and the presence of the major abnormalities in Leads II and III in the former) merely reflects the position of the heart. An appreciation of this fact will allow the ready recognition of the RST-T changes of left ventricular hypertrophy, no matter in what lead they occur. Recourse to the precordial leads will resolve the diagnostic dilemma, especially when right axis deviation is present. Since right axis deviation with inversion of T_2 and T_3 may occur in both right and left ventricular hypertrophy, a study of the precordial leads may reveal the characteristic changes in voltage of the QRS, in the RST-T waves, and in the ventricular activation time in the left precordial leads if left ventricular hypertrophy is present. The typical findings of right ventricular hypertrophy will be noted in Leads V_1 and V_2 if the abnormalities in the standard leads are due to right ventricular hypertrophy.

The data presented on voltage of the QRS complexes in the precordial leads should prove helpful in providing supportive evidence of left ventricular hypertrophy in the early stages of the developing pattern. This is especially true in patients in whom the heart is not horizontal (Fig. 9). The data on voltage provided by Gubner and Ungerleider[10] will be adequate in most cases of left ventricular hypertrophy with horizontal heart. In these patients the voltage

is often equally abnormal in both standard and precordial leads, although exceptions in both directions may occur; the various data on voltage are complementary. In hearts that are not horizontal, even in semihorizontal hearts, we have found abnormal voltage of the QRS in the unipolar left arm lead and/or in the precordial leads (S in V_1 + R in V_5) and yet the voltage in the standard leads ($R_1 + S_3$) was not abnormal. In these cases, the additional information offered by the data on voltage presented here was of definite diagnostic value.*

SUMMARY AND CONCLUSIONS

1. A statistical study is presented of the unipolar precordial and augmented limb leads in 147 cases of left ventricular hypertrophy.

2. The patterns of left ventricular hypertrophy are described with particular attention to the early abnormalities found (depressed RS-T segment with flat or low diphasic T waves, abnormally high voltage of the QRS complex, and delayed onset of the intrinsic deflection).

3. The characteristic and diagnostic changes in the precordial leads found in the cases of left ventricular hypertrophy studied include, in order of frequency:

(a) A depressed RS-T segment and asymmetric inversion of the T wave in Lead V_5 or V_6. In early cases, the T wave may be low and diphasic or flat in association with depression of the RS-T segment.

(b) Abnormalities in voltage of the QRS complex in which the R wave in V_5 or V_6 exceeds 26 mm. and/or the sum of the R wave in V_5 and the S wave in V_1 exceeds 35 mm.

(c) The onset of the intrinsic deflection (the ventricular activation time) exceeds 0.05 second in Lead V_5 or V_6.

4. The same characteristics noted in V_5 and V_6 often appear in aV_L in horizontal hearts and in aV_F in vertical hearts. The changes in these unipolar extremity leads usually are less striking but occasionally may be more abnormal than the changes in the precordial leads.

5. Abnormalities in the left arm lead (aV_L) usually are reflected in Lead I, and the pattern of left ventricular hypertrophy in the standard leads described as "typical" in the literature occurs in individuals with horizontal hearts. The abnormalities seen in Lead aV_L usually are more striking than those found in Lead I.

6. Abnormalities in the left leg lead (aV_F) usually are reflected in Leads II and III, but to a lesser degree. Individuals with abnormalities in these leads have been shown to have vertical hearts and the standard leads will disclose no axis deviation or right axis deviation, and the pattern described in the literature as "atypical" will appear.

7. The diagnostic significance of the voltage of the left ventricular potentials as reflected by the sum of the R wave in V_5 or V_6 and the S wave in V_1 is empha-

*Since this paper was submitted for publication, twenty-two patients in whom the diagnosis of left ventricular hypertrophy was made by the electrocardiographic criteria here presented have been examined at autopsy. In twenty patients the left ventricular thickness equalled or exceeded 1.5 cm. and in the remaining two patients the heart weights were 500 grams and 420 grams, respectively. The left ventricular thickness in these two patients was 1.2 centimeters.

sized. Thirty-two per cent of patients with left ventricular hypertrophy had the sum of these two potentials exceed 35 mm., whereas in no normal person did this sum exceed 35 mm.; in 96 per cent of normal individuals the sum was found to be below 30 millimeters.

8. The voltage of the R wave in V_5 and in aV_L was helpful in the diagnosis of left ventricular hypertrophy. In 20 per cent of the patients with left ventricular hypertrophy, the voltage of R exceeded 26 mm. in V_5 and in 22 per cent this voltage exceeded 10 mm. in aV_L, the maximum values found in normal subjects according to our data.

9. The importance of the time of onset of the intrinsic deflection (ventricular activation time) is discussed. In 35 per cent of patients with left ventricular hypertrophy the ventricular activation time was 0.06 second or more, in contrast to the fact that this delayed time was not encountered in any of 150 normal subjects.

10. In the evaluation of left axis deviation and RST-T abnormalities in the standard limb leads, unipolar extremity and precordial leads are confirmatory and often of critical diagnostic importance.

11. Horizontal or semihorizontal hearts were found in eighty-three (56 per cent) while vertical or semivertical hearts were found in thirty-two (22 per cent) of the patients with left ventricular hypertrophy in this series.

12. Low T waves were frequently noted in Leads V_5 and V_6 in association with tall R waves, resulting in a high R/T ratio. Fifty per cent of the patients in this series had an R/T ratio in V_5 and/or V_6 exceeding the maximum ratio of 10 found in the normal subjects.

The authors wish to express their thanks to Mrs. Suzanne Cahill, Mrs. Doris Tuttle, and Mrs. Angelina Galente for valuable technical assistance. We are also grateful to Dr. John C. Talbot for statistical advice.

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THE VARIABLE LOUDNESS OF THE FIRST HEART SOUND IN AURICULAR FIBRILLATION

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NOT much attention has been given the variable loudness of the first sound which is apparent during auscultation of the heart in patients with auricular fibrillation.[1,2,3] Some clinicians appear to be relatively unaware of the variations, and even books on heart disease offer little or no information. Others, under the impression that loudness varies with strength of ventricular contraction, seem to expect the loudest sounds after the longest diastolic intervals.

The first heart sound also varies in loudness in patients with the regular rhythm of complete A-V heart block, in which the strength of ventricular contractions is virtually constant. In this arrhythmia, studies have shown the relationship of accentuated sounds to short P-Q intervals, and it appears that the loudest sounds are those produced when the onset of ventricular systole finds the auriculoventricular leaflets most widely separated by the jet of rapid flow with auricular systole.[4,5]

It seems reasonable, therefore, that variations of the loudness of the first sound in auricular fibrillation might also find an explanation from an analysis of the relation of the time of onset of ventricular systole to the early diastolic phase of rapid filling.

OBSERVATIONS

Records of the heart sounds at the apex were made during quiet respiration, by means of the device described by Rappaport and Sprague,[6] in twelve recumbent patients with auricular fibrillation. In suitable phonocardiograms the greatest vibration of the first sound was measured for 38 to 160 cycles, with an average of 60 per patient; peak amplitude so obtained was converted from millimeters to arbitrary units, and for each first sound it was plotted against the time in seconds by which the onset of that sound followed the onset of the second heart sound of the preceding cycle (Figs. 1 through 12).

This interval is considered to be a rough index of the desired but unobtainable interval, namely, the interval from the start of the phase of early diastolic rapid filling to the onset of ventricular systole. The latter point must lie between the first deflection of the QRS complex and the beginning of the first sound, while the former probably falls at a more variable point several hundredths of a second

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Received for publication Feb. 18, 1948.

TABLE I. DATA CONCERNING TWELVE PATIENTS WITH AURICULAR FIBRILLATION

	CASE	RECORD NUMBER	AGE	NO. OF CYCLES	MEAN VENTRICULAR RATE PER MINUTE	MEAN INTERVAL: ONSET QRS TO ONSET OF FIRST SOUND (SECONDS)	MITRAL STENOSIS	APICAL SYSTOLIC MURMUR	ARTERIAL PRESSURE (MM. HG) SYS.	ARTERIAL PRESSURE (MM. HG) DIAS.	CONGESTIVE HEART FAILURE	BASAL METABOLIC RATE OR FEVER	OTHER LESIONS
1	F. W.	A25932	56	160	95	0.04	Absent	0	150	90	+++	+43%	0
2	K. D.	243560	45	50	115	0.06	Absent	0	130	85	++	+60%	0
3	L.	—	50	51	85	0.12	Absent	0	200	110	+	–	Left BBB
4	H. W.	239417	27	50	105	0.05	Absent	+	120	90	0	38.5°C.	Aortic stenosis, SBE, recent myocardial infarction
5	J. G.	A95407	55	38	95	L0.06* R0.14*	Absent	0	200	130	±	–	Right BBB
6	M. L.	242633	57	50	70	0.05	Present	++	160	105	+++	–	Aortic stenosis
7	F. S.	208752	58	50	90	0.04	Present	+	160	80	0	+68%	Right BBB
8	S. M.	—	58	50	90	0.04	Present	0	110	80	+	−9%	0
9	H. S.	239886	30	50	100	0.07	Present	++	115	85	++	–	0
10	J. R.	—	39	50	85	0.06	Present	+	130	90	0	–	0
11	L. T.	—	41	69	95	0.04	Present	+	140	90	0	−10%	0
12	R. S.	238118	47	50	60	0.04	Present	+	170	95	++	–	Aortic regurgitation

*See fourth paragraph under "Results" (p. 191) and Fig. 5.

after the second heart sound. Justification for the use of peak amplitude as a measure of loudness has been discussed elsewhere.[4]

Pertinent data regarding the patients are summarized in Table I. The first five patients were thought to have normal auriculoventricular leaflets; the last seven had rheumatic heart disease with mitral stenosis. Case 3 was reported elsewhere[7] as Patient 9, and Case 4 was described as Case 6 in another place.[8] In the figures, the number in the lower left-hand corner corresponds to the case number found in Table I.

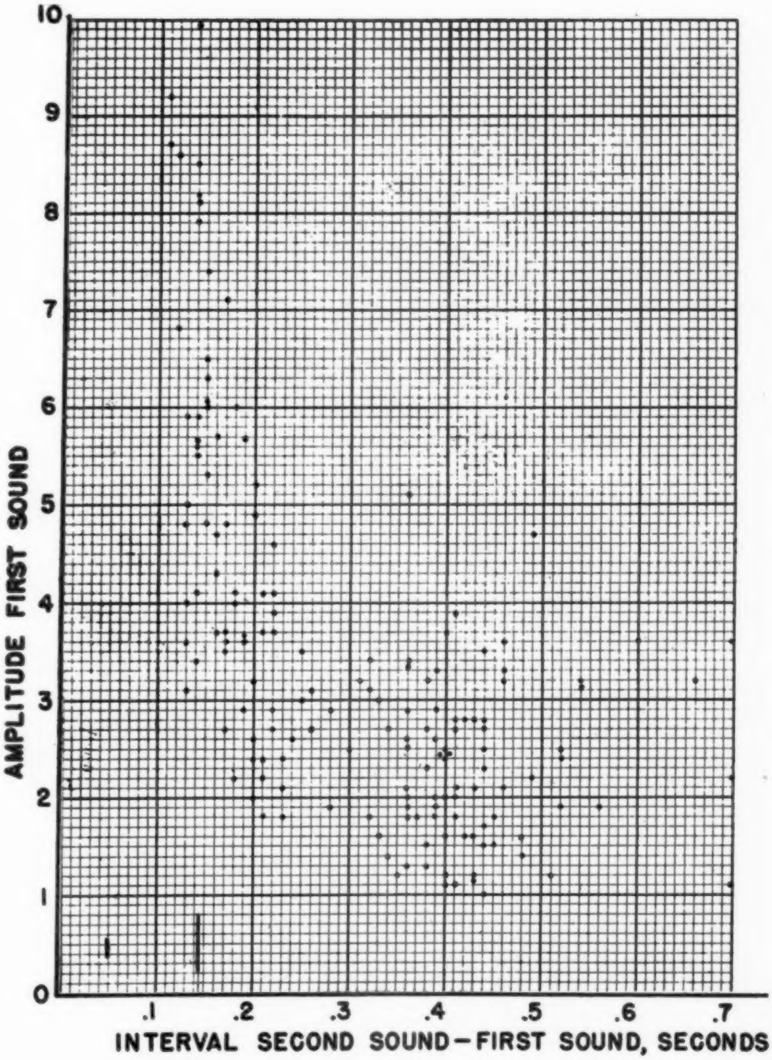

Fig. 1.—Case 1. Peak amplitude (in arbitrary units) of the first heart sound at various intervals after the preceding second sound. Intervals between sounds are from onset to onset. The perpendicular line near lower left corner indicates the position of a gallop. Each dot represents one cycle.

RESULTS

From the data of Figs. 1 through 12, mean peak amplitudes of the first heart sound were calculated in each patient at various time intervals separating the first sound and the preceding second sound (expressed in the legends of the figures as Interval Second Sound—First Sound). Figs. 13 and 14 give the results for Cases 1 through 5 without mitral stenosis, while Figs. 15 and 16 represent Cases 6 through 12 with that lesion. It is clear that variations in the intensity of the first sound depend upon the presence or absence of mitral stenosis.

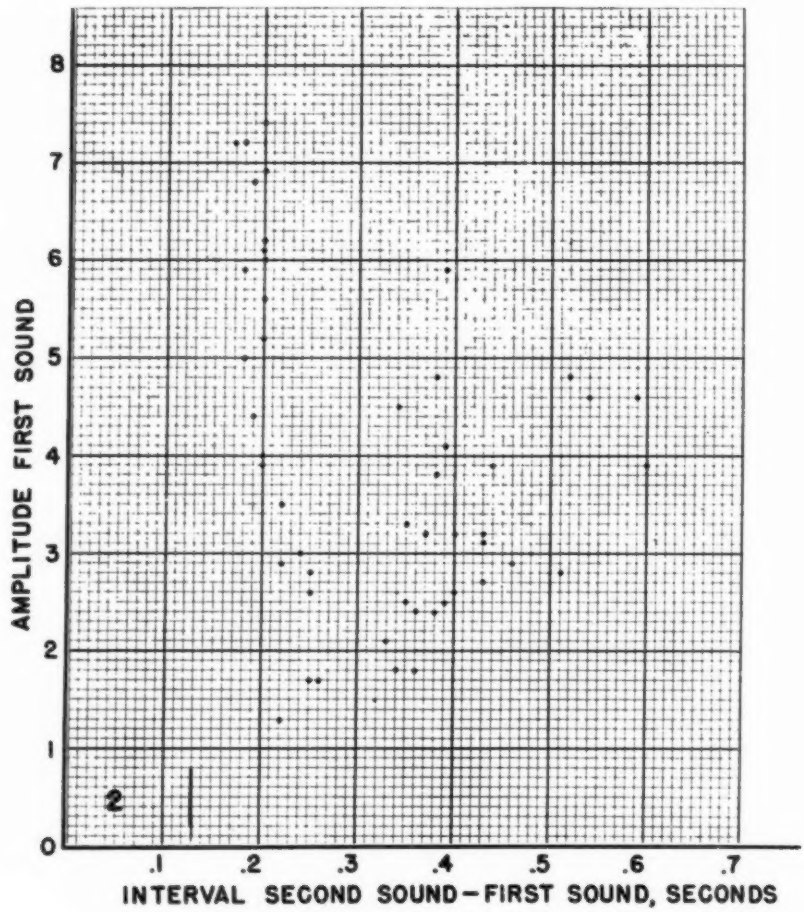

Fig. 2.—Case 2. See legend for Fig. 1.

In Cases 1, 2, and 3 (Fig. 13) there is an early diastolic gallop with congestive heart failure, this sound appearing earlier in Cases 1 and 2 with the rapid blood flow of hyperthyroidism. In each of these cases, as in one reported by Selenin and Fogelson,[1] the period of most intense first heart sounds more or less coincides with the location of the gallop (0.13 to 0.24 second after the start of the second

sound). This is especially striking, having been pointed out before[7] in Case 3; in the curves of this patient there appears to be a phase of fainter first sounds very early in diastole, a phase not found in Cases 1 and 2, perhaps because of the lack of sufficiently early cycles. First sounds occurring after the position of the gallop are seen to become progressively fainter as they appear up to about 0.25 to 0.35 second after the preceding second heart sound. As this interval increases, until the first sound occurs late in diastole, the curves for amplitude of the first sound diverge somewhat: that for Case 1 remains constant at a low level, that for Case 2 shows a gradual increase, and that for Case 3 is intermediate.

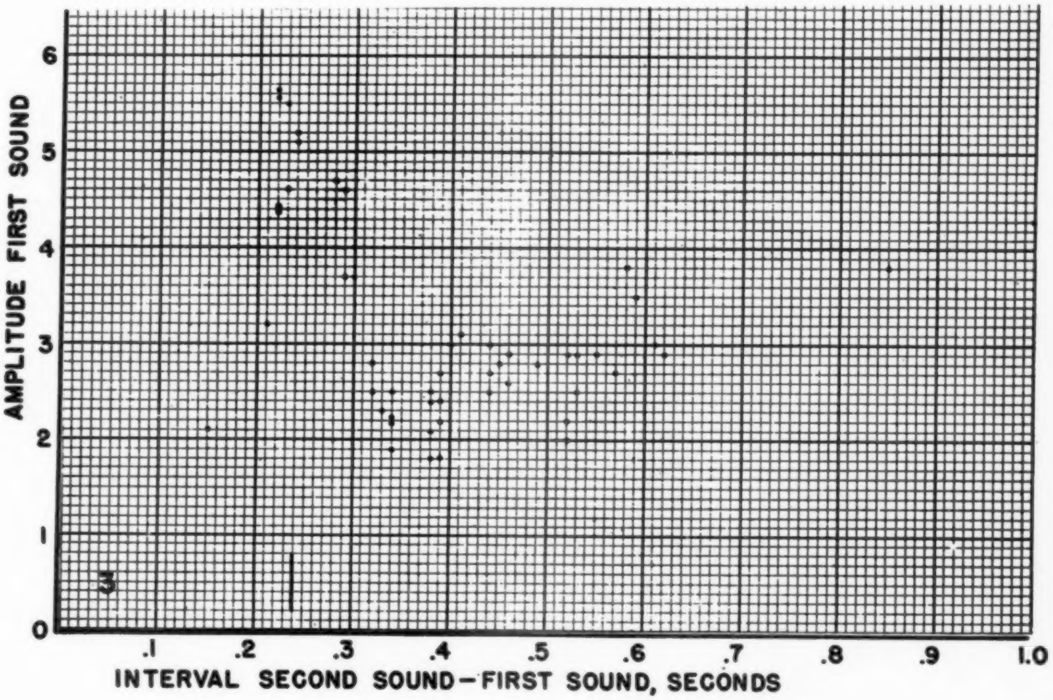

Fig. 3.—Case 3. See legend for Fig. 1.

The curve for Case 4 (Fig. 14) shows a greater increase of amplitude in late diastole. It otherwise resembles those in Fig. 13, with one exception: early in diastole, there appear to be two separate groups of sounds (the two broken lines of Fig. 14). This division seems to be determined by the length of the preceding cycle; the five louder sounds (Fig. 4) were preceded by R-R intervals of 0.42 to 0.50 second (mean, 0.46) and the seven fainter ones by R-R intervals of 0.55 to 0.70 second (mean, 0.60). An observation similar to this has been made by others.[2]

In Case 5 simultaneous records of carotid pulse and heart sounds confirmed the electrocardiographic demonstration (broad S wave in the first lead) of right bundle branch block. It was therefore possible to identify the early component

of the split first sound as a left-sided event and the late component as a right-sided event[9]; since the components of the split second sound were also identifiable, each element of the first sound was studied in relation to its ipsilateral element of the second sound. Figs. 5-*L* and 14 show that the peak amplitude of the left-sided first sound behaves much as it did in Cases 1, 2, 3, and 4. Fig. 5-*R*, on the other hand, shows no relationship between the right-sided first sound and its position in diastole.

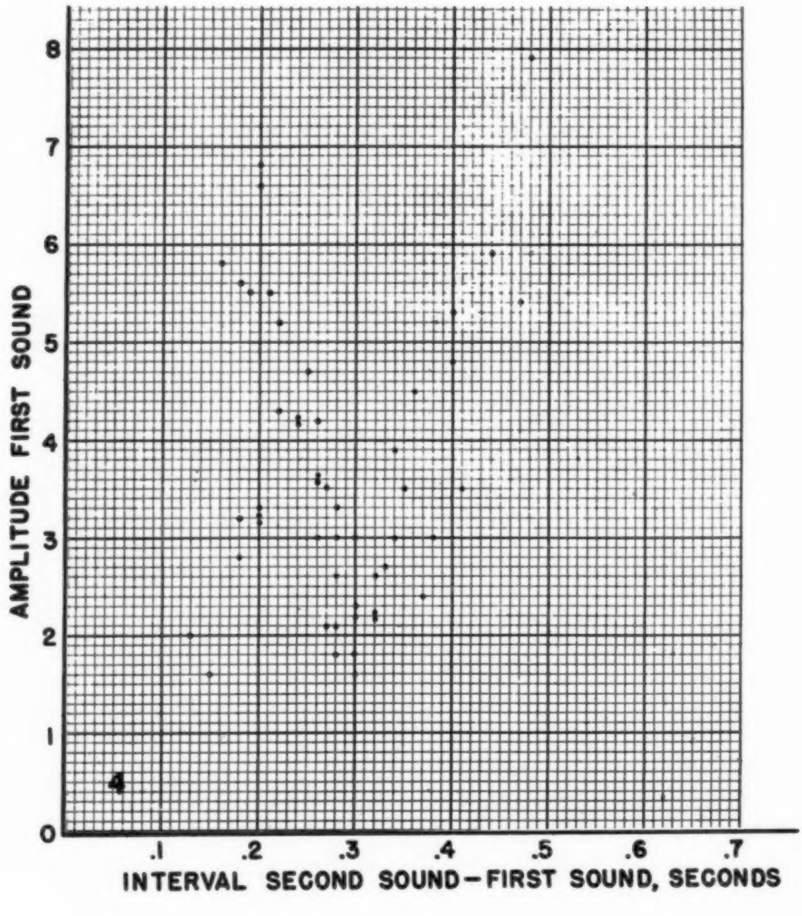

Fig. 4.—Case 4. See legend for Fig. 1. There was no gallop.

In general, then, the peak amplitude of the first sound in patients with auricular fibrillation, but without mitral stenosis, follows this pattern: it is greatest when its onset falls soon after the preceding second sound, at a time coinciding with that of the gallop (if present); it then diminishes quickly through the next tenth of a second to values 23 to 44 per cent (mean, 37) of its early height;

later in diastole it may continue at this low level (Case 1) or increase again toward (Cases 2, 3, and 5) or even beyond (Case 4) the high early magnitude.

The results in patients with mitral stenosis are very different. In Cases 6, 7, and 8 (Fig. 15) there may be a slight gradual decline as the first sound occurs

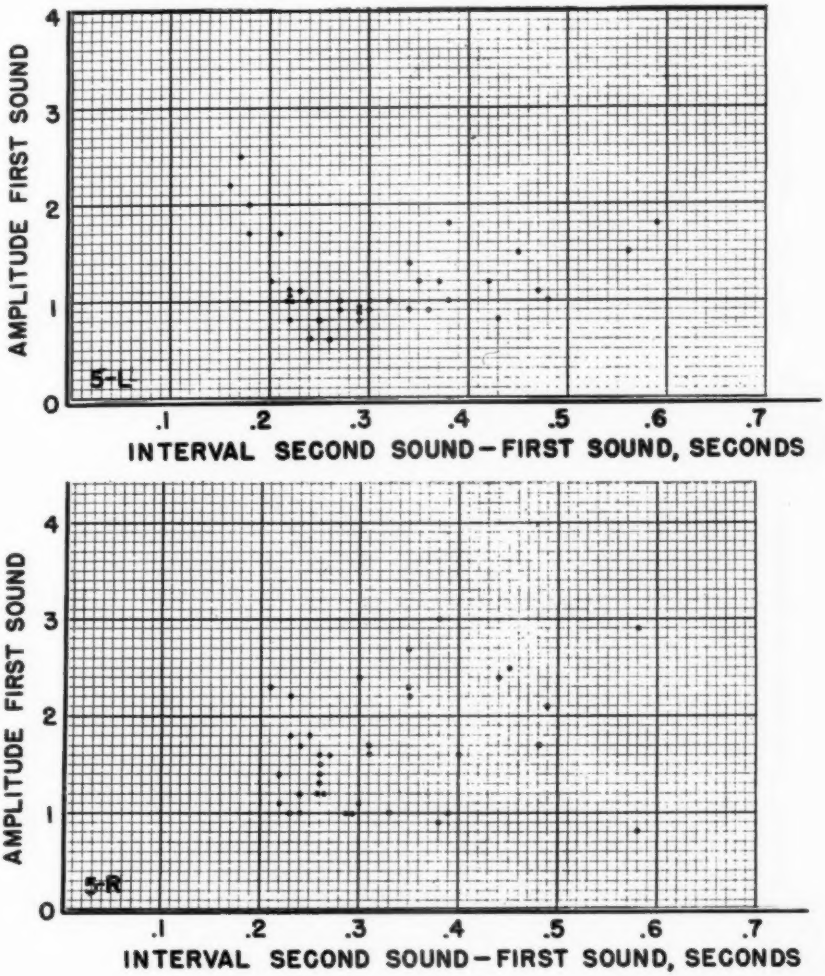

Fig. 5.—Case 5. See legend for Fig. 1. Each component of split first and second sounds could be identified in this patient with right bundle branch block. Fig. 5-*L* (above) gives the left-sided sounds; Fig. 5-*R* (below) gives those from the right.

progressively later in diastole, but the changes are not impressive. In Cases 9, 10, 11, and 12 (Fig. 16) there appears to be a zone of moderate accentuation about 0.4 to 0.6 second after the last second heart sound, with less intense first sounds both earlier and later. While the number of very early cycles available for study was not as great as could be desired, there is no doubt, in Cases 8 and 11,

at least, of the relative faintness of the first sound when it occurs during the period of the murmur.

On the whole, these patients with mitral stenosis showed relatively little variation in amplitude of their first sounds. This was noted earlier by Wolferth and Margolies.[2]

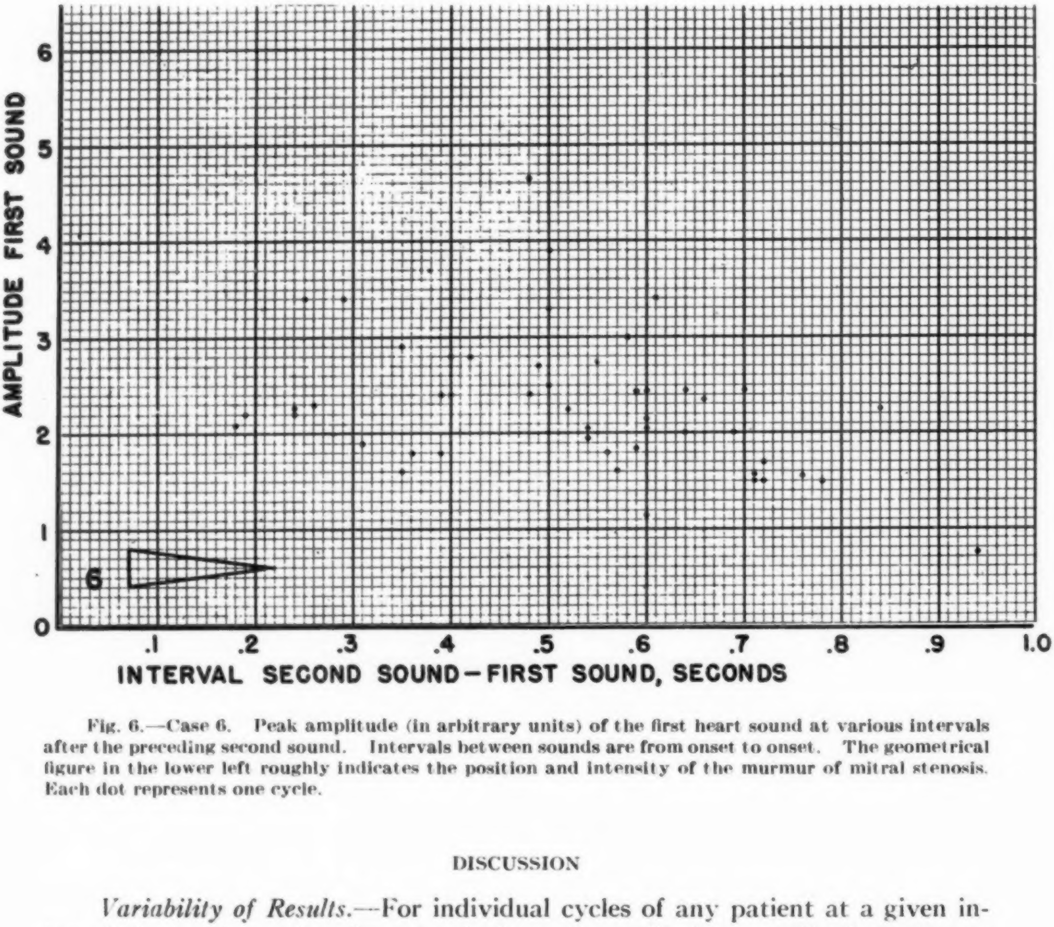

Fig. 6.—Case 6. Peak amplitude (in arbitrary units) of the first heart sound at various intervals after the preceding second sound. Intervals between sounds are from onset to onset. The geometrical figure in the lower left roughly indicates the position and intensity of the murmur of mitral stenosis. Each dot represents one cycle.

DISCUSSION

Variability of Results.—For individual cycles of any patient at a given interval of second sound to first sound, the peak amplitude generally showed more variability than was found when amplitude and P-Q intervals were correlated in patients with complete A-V heart block.[4] This may be the result of irregular rhythm with different cycle lengths preceding beats at identical second sound-first sound intervals, as suggested by the findings in Case 4. Another possibility might be found in simultaneous effects of respiration on amplitude and heart rate, or on cardiodynamics.[10,11] In any event, the means (Figs. 13 through 16) yield consistent results and are probably reasonably reliable.

It is also appreciated that with the irregular rhythm of auricular fibrillation certain variables are introduced which were not a problem in similar studies on

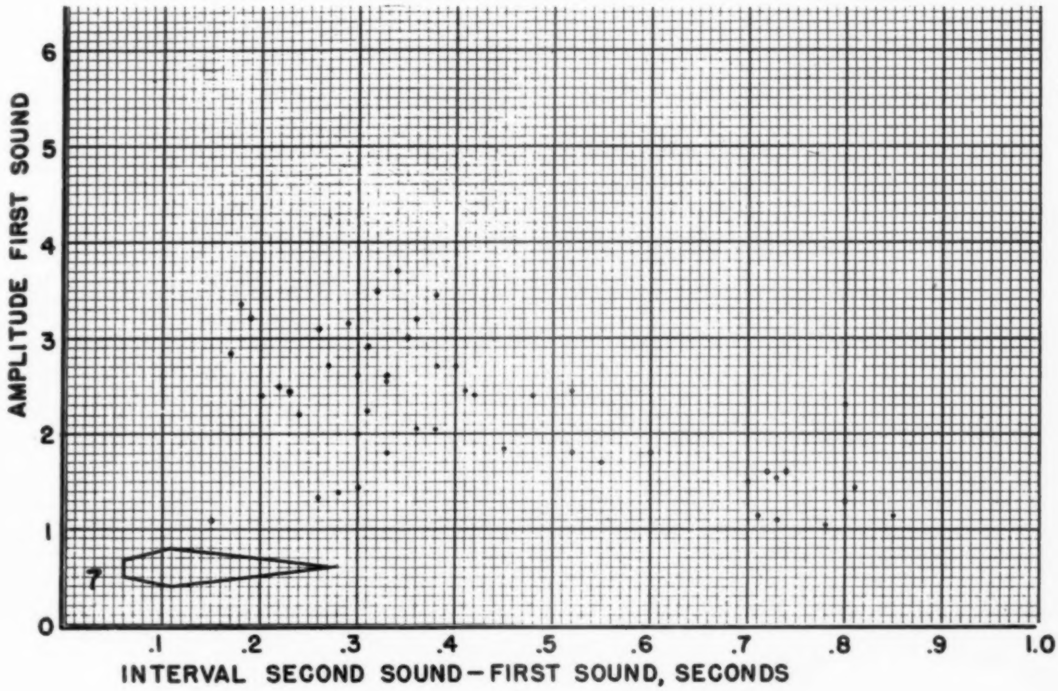

Fig. 7.—Case 7. See legend for Fig. 6.

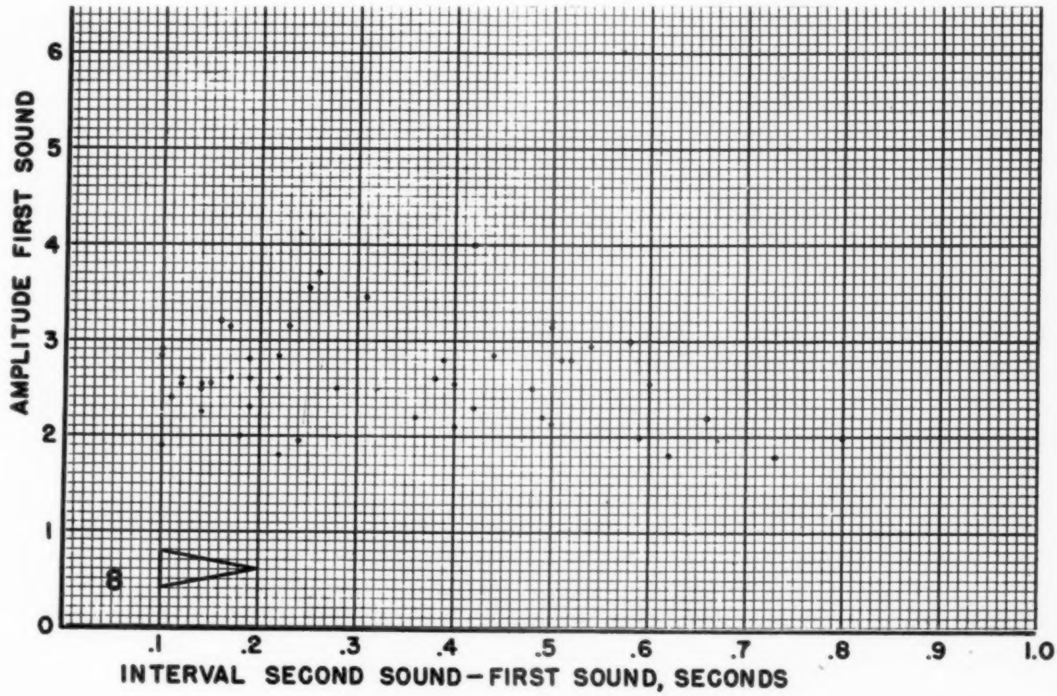

Fig. 8.—Case 8. See legend for Fig. 6.

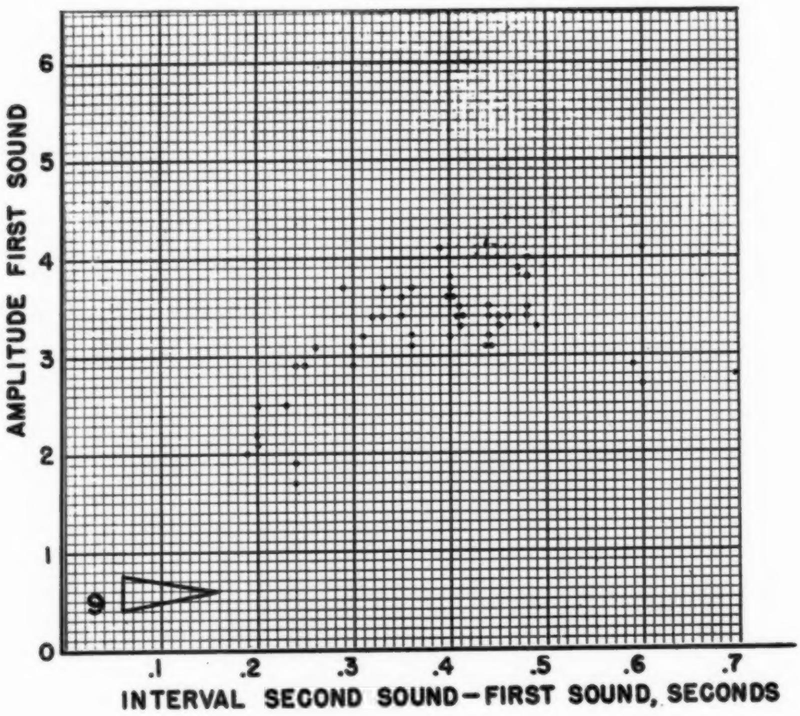

Fig. 9.—Case 9. See legend for Fig. 6.

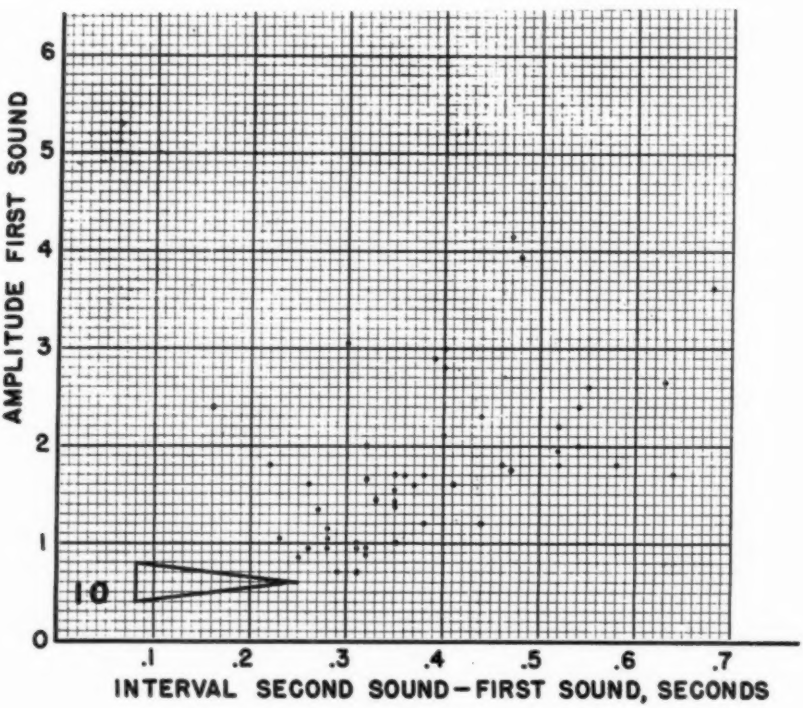

Fig. 10.—Case 10. See legend for Fig. 6.

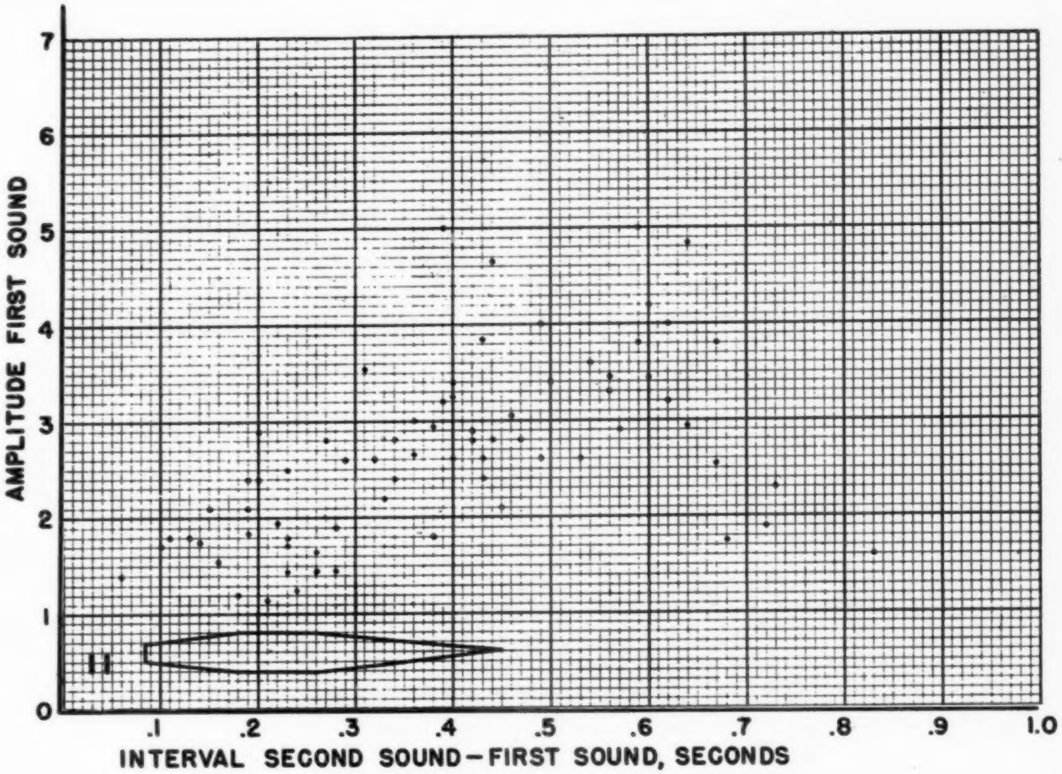

Fig. 11.—Case 11. See legend for Fig. 6.

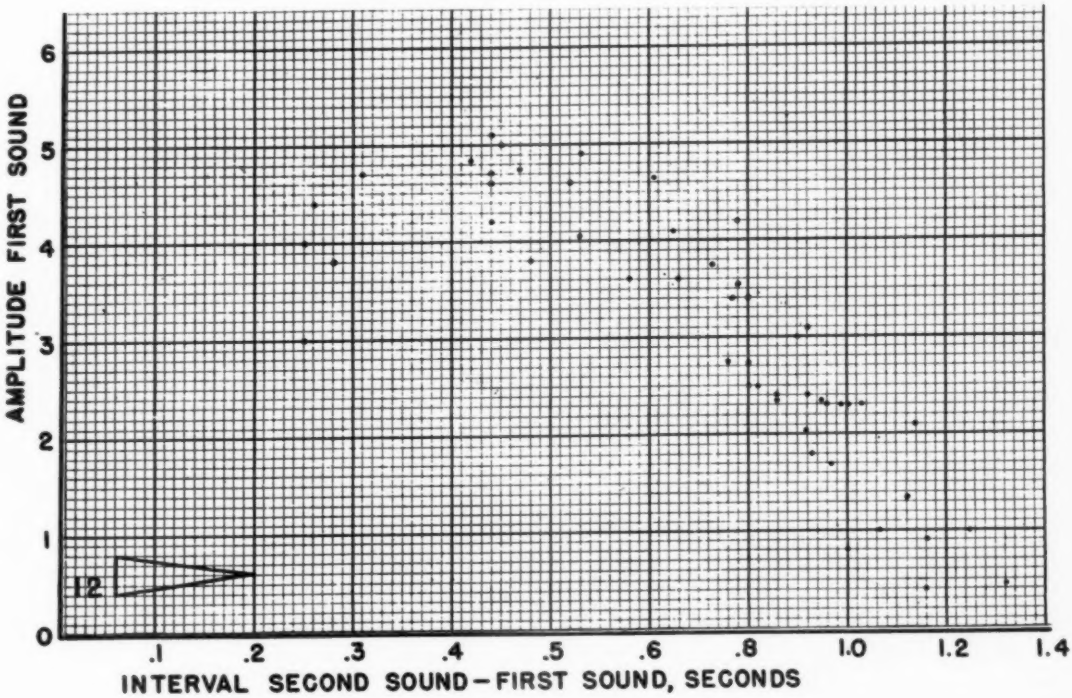

Fig. 12.—Case 12. See legend for Fig. 6.

the first sound in complete A-V heart block.[4,5] Thus, the interval of second sound to gallop shortens with shorter preceding cycles[12]; the intervals of onset of QRS to ejection[13] and QRS to first sound[3] shorten after longer diastoles, and with short diastoles, the pulse and systolic arterial pressures are diminished while the

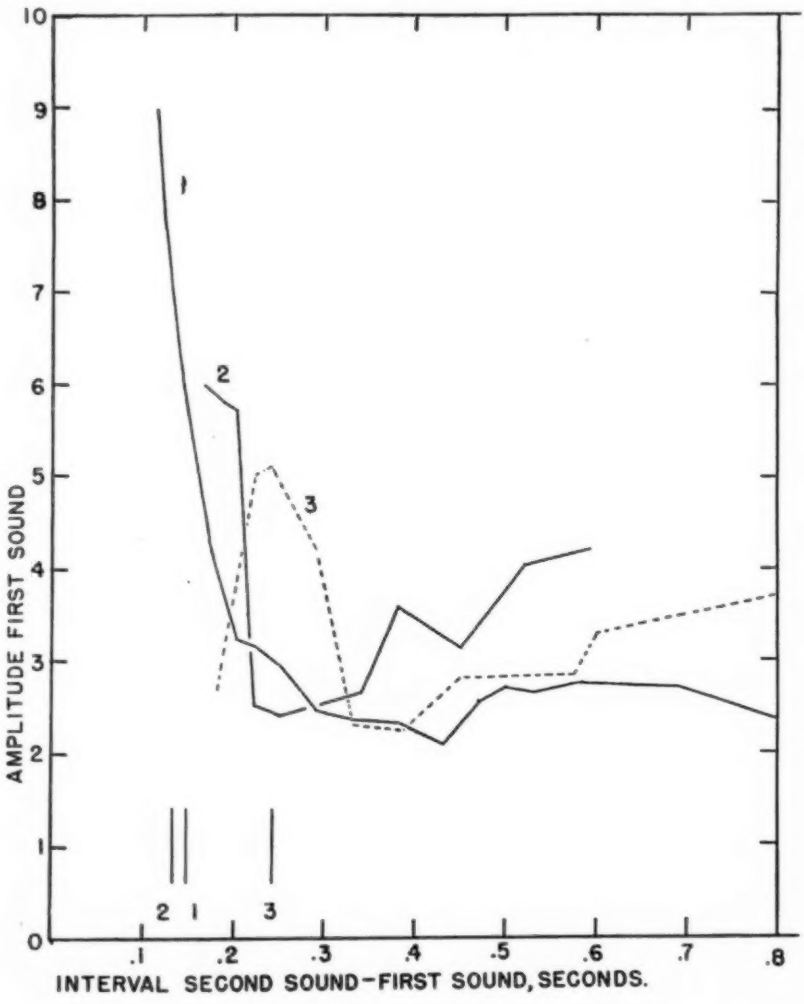

Fig. 13.—Cases 1, 2, and 3 without mitral stenosis. Variation of mean peak amplitude of first heart sound at different intervals between the onset of that sound and the onset of the preceding second sound. Respective gallops indicated at left below.

diastolic arterial pressure is increased.[13] Only the first of these is directly pertinent to the present study; an attempt at correction proved too cumbersome and was abandoned with the hope that the fairly large number of cycles studied would cancel this factor.

Normal Mitral Leaflets.—In the absence of mitral stenosis and when sufficient data are available (Case 3), the curve of peak amplitude of the first sound plotted against length of diastole in auricular fibrillation closely resembles that for the same variable plotted against P-Q intervals in complete A-V heart block.[4]

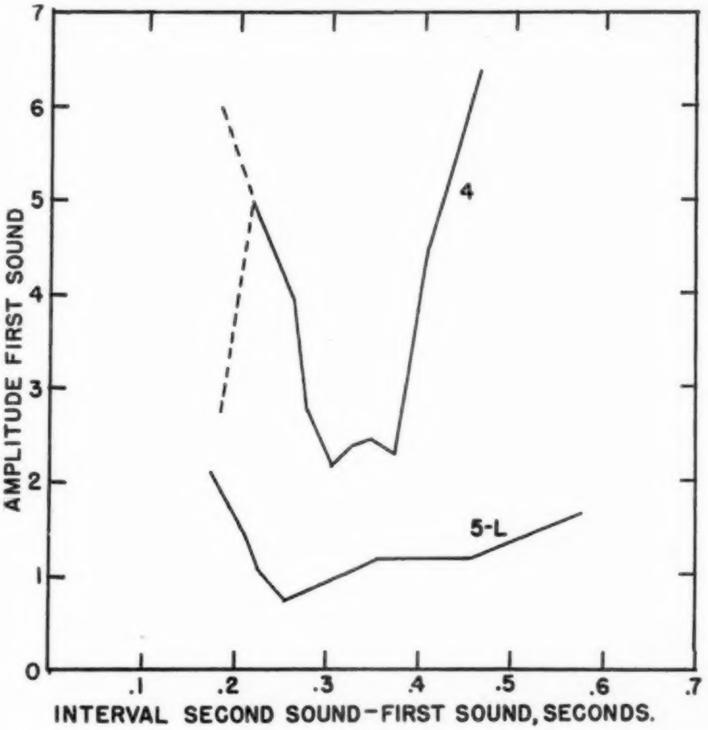

Fig. 14.—As in Fig. 13. Case 4 and the left-sided sounds of Case 5.

The resemblance goes so far as to include different degrees of secondary zones of accentuation at times relatively long after the respective (early diastole or auricular systole) rapid filling phases. As was the case in most of the elderly patients with heart block, there was no such zone at all in Case 1 (56 years of age) after long diastoles. Since systolic and pulse pressures have been shown invariably to rise with increasing diastole,[13] this finding is one more point against the determination of the loudness of the first sound by strength of ventricular systole.[4] The greatest degree of secondary (late) accentuation was observed in the youngest patient, Case 4; this is clearly analogous to similar great increases in young children with complete heart block.[4,14] It should be noted that secondary accentuation, late in diastole, was regularly found in this study in subjects as old as 45 to 55 years; on the other hand, a similar late zone of accentuated first sounds after auricular systole was the exception in patients with complete

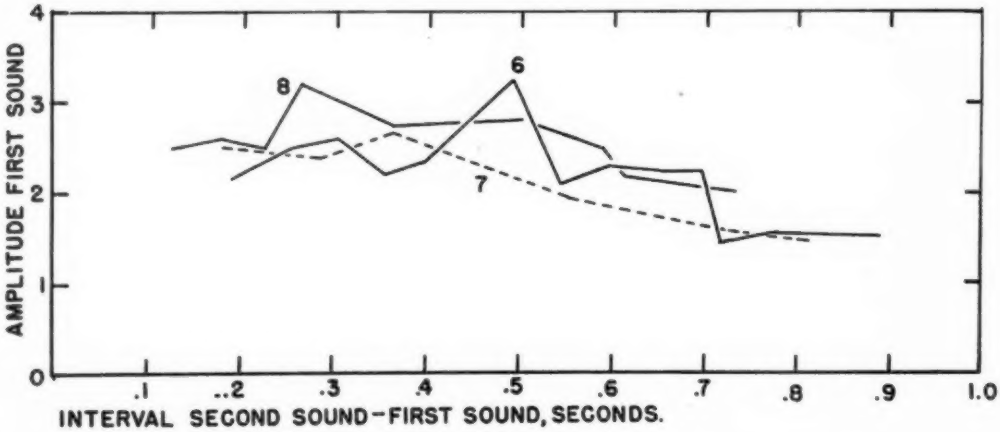

Fig. 15.—As in Fig. 13. Cases 6, 7, and 8 with mitral stenosis.

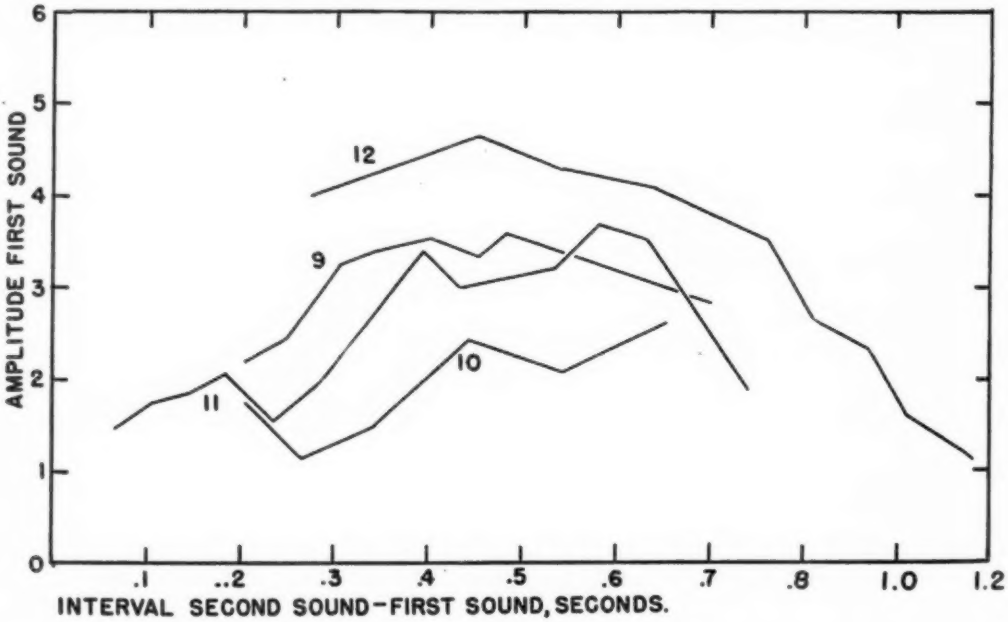

Fig. 16.—As in Fig. 13. Cases 9, 10, 11, and 12 with mitral stenosis.

heart block above the age of 14 years.[4,14] The significance of such a discrepancy in age limits is not clear.

Finally, the comparison includes the coincidence of the periods of greatest first sound vibrations with times at which other sounds occur. This is not simply the result of adding sounds together,[4] but must have something to do with the mechanism of sound production. With auricular fibrillation, the loudest first sounds and the early diastolic gallop (Cases 1, 2, and especially 3) appeared to come at the same interval after the second heart sound; with heart block, the loudest first sounds and the first component of double auricular sounds seemed to appear simultaneously after the P wave.[4]

In other places[4,5,15] there was presented evidence confirming earlier views[16,17] that the loudest first sounds in complete heart block are those produced when the onset of ventricular systole finds the auriculoventricular leaflets most widely separated following auricular systole. Dean's[18] basic observations on the movements of the septal cusp of the mitral valve after auricular contraction (perfused cat's heart) have been frequently quoted and are experimental evidence compatible with the foregoing statement. The same worker also found similar movements, but of less magnitude, in early diastole: "synchronous with [ventricular] relaxation the valves open quickly, moving down to a lower position than they occupied before the onset of systole. From this point they are slowly buoyed upward as blood flows into the ventricle from the auricle during the remainder of diastole."[18] It therefore appears that, regardless of the irregular rhythm and inconstant strength of ventricular systole with auricular fibrillation, the loudest first heart sounds coincide with the widest opening of normal auriculoventricular valves just as in complete heart block. This relationship actually gives the loudest sounds early in diastole in spite of weaker ventricular contractions at that time.

Mitral Stenosis.—With mitral stenosis, there was no period of accentuated first heart sounds when ventricular systole occurred early in diastole. On the contrary, the first sound in some of the patients (Figs. 15 and 16) was of appreciably diminished amplitude when it interrupted the early diastolic murmur.

This is evidence against the suggestion[16] that the loud, snapping first sound in mitral stenosis with sinus rhythm is chiefly the result of prolongation of the peak of auricular systole. Such prolongation probably occurs, to be sure, but by comparison with the present results in the early diastolic rapid filling phase, one might then expect a faint first sound. It is more likely that the typical first heart sound of mitral stenosis is related to altered sound production by the diseased leaflets because of their rigidity and thickness, in spite of their semiclosed aperture.

In fact, if one accepts the hypothesis that the first sound is relatively louder if ventricular systole begins when the A-V leaflets are wider apart, and vice versa, the present findings suggest narrowing of the mitral orifice at the time when flow is presumably greatest coincident with the murmur of early diastole. This apparent paradox may find its explanation in the venturi effect: the velocity of flow might be so great through the narrow opening that lateral pressure would

fall, with resultant further narrowing if the orifice were capable of any changes in size. Velocity through a normal mitral aperture does not appear to be great enough for this principle, but Hochrein[19] demonstrated it for normal semilunar valves during the phase of rapid ejection; with aortic stenosis the venturi effect is thought to be magnified.[20]

In the present study, the absence of relatively accentuated first heart sounds early in diastole in patients with mitral stenosis merits further consideration. Tricuspid stenosis was not thought to be present in any of the subjects. If accentuation occurs when either tricuspid or mitral leaflets are widely separated at the onset of the appropriate ventricular systole, why did not the normal tricuspid valve produce accentuation regardless of the apparent inability of the stenotic mitral valve to do so? The most simple explanation might hold that any variation in amplitude arising from the tricuspid valve would be submerged in the typically loud, snapping sound of mitral stenosis, and this is probably an important factor.

It is also conceivable that the range of variation in amplitude capable of production by the right side of the heart is less than that on the left side, a conception compatible with the contrast in size (and probably range of motion) between the septal mitral cusp and all other auriculoventricular leaflets. In a study of the variable amplitudes of both elements of the split first sound in a patient with heart block, Wolferth and Margolies[21] found "the extent of the variations in the second component are not nearly so great as those of the first component," but the presence of right bundle branch block was not established in that subject (Case II); in their other subjects, with less widely split first sounds, such striking inequalities were not present. In the present studies, the first sound was split only in Case 5. In this patient, variable amplitude could be demonstrated on the left side but not on the right; however, the data are not considered adequate to settle the question.

A short time ago an apical blowing murmur during ventricular diastole was described in elderly patients with heart block, together with reasons for believing that mitral stenosis was not present.[22] Further observations in some of those patients suggested that the murmur was produced while the auriculoventricular leaflets were closing, toward the end of auricular systole.[4] The present studies are regarded as additional evidence that mitral stenosis did not cause the murmur in those patients, for analyses of the variable amplitudes of their first heart sounds indicated that the movements of their auriculoventricular leaflets were quite similar to those of other elderly patients with heart block but without the murmur.[4]

Finally, the results have a diagnostic implication. It is sometimes difficult to decide whether an apical diastolic rumble is present in a patient with auricular fibrillation and rapid ventricular rate; the occurrence of relatively accentuated first sounds after the shorter diastolic pauses should weigh against the presence of mitral stenosis. At slower rates there may be no cycles short enough to yield the accentuation typical of normal leaflets, but under these conditions the murmur of mitral stenosis is ordinarily audible when that lesion is present.

The present series of patients is inadequate in number to permit full evaluation of the possible usefulness of this point.

SUMMARY AND CONCLUSIONS

From phonocardiograms recorded in twelve patients with auricular fibrillation, peak amplitude of the first heart sound (as an index of loudness) was measured in 718 cycles and correlated with the preceding interval: second sound to first sound (as an indirect measure of time in the early diastolic rapid filling phase).

In five patients without mitral stenosis, the first sound usually had the greatest peak amplitude when its onset came 0.12 to 0.24 second after that of the preceding second sound; this period coincided with the presence of an early diastolic gallop in three cases. Falling during the next tenth of a second to about one-third of its earlier highest magnitude, peak amplitude with longer diastoles either remained diminished or had a secondary zone of accentuation.

These changes of peak amplitude at varying times in the early phase of rapid filling are very much like those of the same variable during and after auricular systole in patients with complete heart block. They are further evidence that the first heart sound is louder when the onset of ventricular systole finds the auriculoventricular leaflets wider open, even though the strength of contraction be weaker.

In seven patients with mitral stenosis there was relatively little variation in peak amplitude of the first heart sound at different times in diastole. If anything, its magnitude was less when the first sound interrupted the murmur of early diastole.

When auscultation is indecisive in a patient with auricular fibrillation and rapid ventricular rate, the finding of intensified first heart sounds after the shorter diastolic pauses would appear to be a point against the presence of mitral stenosis.

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III. CORRELATION OF ELECTROCARDIOGRAPHIC AND PATHOLOGIC FINDINGS IN ANTEROPOSTERIOR INFARCTION

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COEXISTENT infarction of the anterior and posterior walls of the left ventricle is a fairly common pathologic finding in persons dying from vascular disease. In some of the cases, the involvement of opposite walls is the result of two or more distinct lesions, as evidenced either by anatomical separation or by differences in age. In other cases, an infarct of uniform age is found in the apical one-third or more of the anterolateral wall and continues through the septum and around the tip of the left ventricle into the apical portion of the posterior wall.[1] Simultaneous infarction of the anterior, lateral, and posterior aspects of the apex may result from occlusion of the anterior descending coronary artery, because of the fact that this vessel frequently passes around the tip of the left ventricle to supply the posteroapical wall.

Electrocardiographic correlations have been reported in relatively few cases with pathologic evidence of coexistent anterior and posterior infarction,[1-14] and, in most of these, the studies were limited to the standard limb leads and to one or two precordial leads. The classical findings in the standard leads consist of abnormal Q waves in all three leads, accompanied early by elevation of the RS-T segment, greater in Lead II than in Leads I or III, and later by inversion of the T waves throughout.[1] The foregoing classical pattern is found in only a small minority of the cases and is not pathognomonic of anteroposterior infarction, since it may be duplicated by posterolateral infarction[15] and perhaps also by anterolateral infarction when the heart is in the vertical position.[16,17] Incomplete patterns characterized by Q waves in either Lead I or Leads II and III accompanied by elevation of the RS-T segment in all three leads may occur as a result of a localized anterior or posterior infarction complicated by generalized pericarditis,[18,19] whereas simultaneous inversion of the T waves in all three standard limb leads may occur under a variety of circumstances.[20]

The infrequence of Q-wave and T-wave abnormalities in all three standard leads is probably due to the tendency for the effects of the anterior and the posterior infarcts to cancel out one another in Leads I and III.[1] The recognition of the combined lesion is aided by even one or two supplementary precordial leads. The signs of the posterior infarct tend to appear in Leads II and III and

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Received for publication Feb. 24, 1948.

those of the anterior infarct, in the precordial lead,[1,5,7] whereas rarely the reverse is observed.[5] In many cases, however, only one of the two lesions can be recognized from a limited number of precordial leads, in addition to the standard leads, and in a few cases neither can be definitely diagnosed.[7-10] A previous study[21] indicated that multiple precordial and unipolar extremity leads supply valuable supplementary data for the diagnosis of coexistent anteroposterior infarction. Although the value of multiple precordial leads, in addition to the customary limb leads, was also brought out in a recently reported group of five cases of pathologically established anteroposterior infarction,[22] there appeared to be a need for an evaluation of the electrocardiographic findings in a larger series.

The purpose of this communication is to present an analysis of the findings in the multiple precordial leads of Wilson and in the standard limb leads and the augmented unipolar extremity leads of Goldberger in fifty-two cases with pathologic evidence of coexistent infarction of the anterior and posterior walls of the left ventricle. This series includes all of our cases in which the foregoing twelve leads were obtained during life and the presence of infarction demonstrated at autopsy in the apical one-third or more of both the anterior and posterior walls of the left ventricle. These fifty-two cases of coexistent infarction of the anterior and posterior aspects of the left apex were encountered in a consecutive group of 161 cases of pathologically localized infarction and represent an incidence of 32.3 per cent.

In twenty of the cases, a recent infarct was found in the apical one-half or more of the anterior wall, which continued through the septum and around the tip of the left ventricle into the apical one-third or more of the posterior wall; in sixteen others, an old, healed infarct of similar distribution was found. The involvement of the anterior and posterior walls was attributed to a single lesion in nineteen of the twenty cases with recent infarction because of the anatomical continuity and the uniformity in age. Simultaneous anteroposterior infarction had probably occurred in most of the sixteen cases with a healed lesion of similar distribution, but confluence of two independent infarcts was established in two cases and could not be excluded positively in some of the remainder. In five additional cases of the series, a continuous anteroposterior apical infarct of uniform age, complicated by a separate infarct of the posterobasal wall, was found. Separate infarcts were found in the anterior and posterior walls in the remaining eleven cases.

The method of clinical and pathological study has been described.[23] In this report, eighteen of the cases of anteroposterior infarction will be presented and analyzed in detail and the findings in all fifty-two cases will be classified and summarized.

CASE REPORTS

CASE 51.—A 40-year-old woman was first admitted to the hospital on Jan. 24, 1944, suffering from hypertensive encephalopathy complicated by moderate left ventricular failure. She had had exertional dyspnea during the preceding year, but denied thoracic pain. After a slow convalescence, she was fairly comfortable until the spring of 1945, when she began to have angina pectoris. In May, 1945, she had a prolonged attack of retrosternal constriction, followed by congestive failure, which kept her incapacitated at home until she was readmitted on Oct. 30, 1945, because of a cerebral hemorrhage. She died in coma three days later.

Electrocardiographic Findings.—Electrocardiograms of Jan. 25, 1944, Feb. 3, 1944, and Oct. 31, 1945, are reproduced in Fig. 1, *A*. The patient had received 0.8 mg. of Cedilanid prior to the first electrocardiogram and was taking digitalis in maintenance doses at the time of the second and third tracings. The initial deflection in all precordial leads of the first two tracings was upright. The abnormally deep and slightly broadened S wave in Leads V_1 and V_2 and the tall R

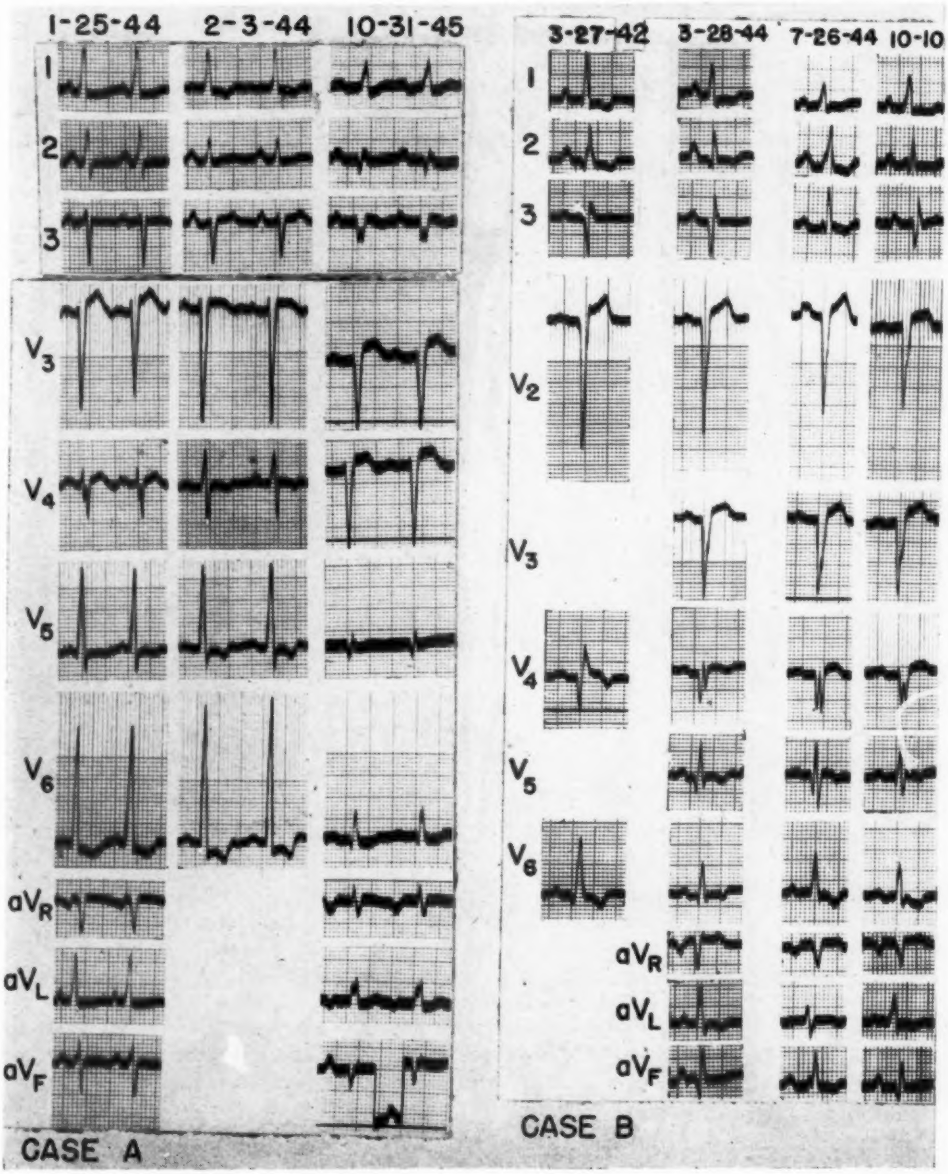

Fig. 1.—Serial electrocardiograms in anteroposterior infarction.

A, Case 51, showing development of signs of anteroposterior infarction between Feb. 3, 1944, and Oct. 31, 1945.

B, Case 52, showing evolution of electrocardiographic signs.

wave in V_5 and V_6 and the slightly delayed onset of the intrinsicoid deflection in V_6 and aV_L were indicative of left ventricular hypertrophy. The elevated RS-T junction in Leads V_1 and V_2 and the depressed RS-T junction with inverted T wave in V_5 and V_6 were the expected findings in left ventricular hypertrophy, but were difficult to evaluate in this case because of the administration of digitalis. It is noteworthy that Lead aV_F on the same date displayed a prominent initial R wave. The final tracing on Oct. 31, 1945, showed marked changes in the pattern of the QRS complex both in the precordial and extremity leads. The replacement of the tall R waves in V_5 and V_6 by abnormal QR complexes was diagnostic of infarction of the subendocardial portion of the anterolateral wall. The marked decrease in the amplitude of the initial R wave in Leads V_3 and V_4 suggested patchy infarction of the anterior wall, and the disappearance of the R waves from V_1 and V_2 suggested that the infarct extended into the septum. Right ventricular dilatation was regarded as a possible, but less likely cause of the QRS changes in the first four precordial leads. The alterations in the RS-T segment and T wave were attributable to digitalis. The reduced voltage and coarse notching of the R wave in Lead aV_L represented probably a different manifestation of the lesion in the lateral wall. The appearance of a prominent initial R wave in Lead aV_R was probably secondary to the large anterolateral infarct. The large initial upstroke formerly present in Lead aV_F was replaced by a Q wave which terminated in a minute notched R wave, 1.0 mm. in amplitude. This change in Lead aV_F, which was carried over into standard Leads III and II, indicated that the infarct involved the posterior aspect of the apex as well as the anterolateral wall. From the available tracings, it was evident that this infarct had developed some time between Feb. 3, 1944, and Oct. 31, 1945, but a more precise estimate of the time of onset was impossible electrocardiographically because of the lack of serial records during 1945. From the history, it would appear that the infarct had occurred in May, 1945.

Pathologic Findings.—The heart weighed 649 grams and exhibited an old, healed infarct, involving the subendocardial three-fourths of the anterolateral and posterior aspects of the left ventricle and the left side of the interventricular septum in the apical three segments and the subendocardial one-third of the anteroseptal wall and left side of the septum in the fourth segment. The position and size of the lesion were thus similar to that in Case 65 (Fig. 12), except that the infarct extended into the subendocardial portions of the lateral and the posterior walls in the third segment in this case in a fashion similar to that which had occurred in the second segment of Fig. 12. There was also a small area of subendocardial infarction in the anteroseptal region of the fifth segment, as in Fig. 12. The infarct was judged to be several months of age and showed no evidence of recent activity. Thus, there was close correspondence between the position of the infarct as predicted from the electrocardiogram and the actual findings at autopsy. The infarction of the subendocardial three-fourths of the anterolateral aspect of the apex accounted for the changes in Leads V_5 and V_6 and the infarction of the posterior aspect of the apex accounted for the changes in Lead aV_F. The lesion of the left side of the septum was apparently responsible for the disappearance of the R wave from Leads V_1 and V_2, and the lesion of the free portion of the anteroseptal wall, for the reduction in the R wave in Leads V_3 and V_4.

CASE 52.—A 64-year-old man was first admitted to the hospital in March, 1942, because of an attack of prolonged retrosternal constrictive pain accompanied by dyspnea. The patient had been almost totally incapacitated ever since then because of recurrences of retrosternal oppression and dyspnea upon the slightest exertion. He was rehospitalized in congestive failure on several occasions during the next two and one-half years and finally died on Oct. 20, 1944.

Electrocardiographic Findings.—The electrocardiograms reproduced in Fig. 1, *B* were selected from a large series taken over a period of two and one-half years, during which the patient was on maintenance doses of digitalis. The abnormal QR pattern in Lead V_4 on March 27, 1942, was typical of anterior infarction and the deep Q wave of Lead III, together with the Q wave and markedly slurred upstroke of the R wave in Lead II, indicated coexistent posterior infarction. Changes in the RST-T complex of Lead V_4 and Leads II and III in serial tracings during March and April of 1942 indicated organization of a simultaneous anteroposterior infarct. From a study of the remaining tracings, it was concluded that no appreciable extension of the infarct had occurred since April, 1942. The location of the infarct is better appreciated through the multiple leads of the electrocardiograms taken in 1944. A small initial R wave was consistently

present in Lead V_1 and was occasionally detectable in Lead V_2. The usual finding in both V_2 and V_3 was a QS deflection. The upstroke of the W-shaped complex of Lead V_4 usually fell short of the isoelectric line, but in some tracings crossed it to form an R wave. The findings in Leads V_2, V_3, and V_4 were attributed to incomplete transmural infarction of the anterior wall. The original cove-shaped inversion of the T wave in Lead V_4 eventually disappeared. Lead V_5 displayed an initial Q wave which ranged from 55 per cent down to 15 per cent of the amplitude of the succeeding R wave and was attributed to extension of the infarct subendocardially into the anterolateral wall. The original Q wave in Lead V_6 subsequently disappeared. In the tracings of March 28 and Oct. 10, 1944, the heart was in an intermediate position electrically and Lead aV_F displayed a broad, slurred Q wave which was more than 50 per cent of the R wave in the same lead. This pattern was typical of posterior infarction and was carried over into Leads II and III. In the tracing of July 26, 1944, however, the heart had shifted into a more vertical

Fig. 2.—Roentgenogram of injected heart in Case 52.

position and a coarse notch at the base of the upstroke of the R wave had replaced the Q wave of Leads aV_F, II, and III. The findings on July 26, 1944, pointed to a conduction defect in the posterior wall, but were not diagnostic of posterior infarction. These last three tracings thus illustrate the postural variations which may occur in Leads aV_F, III, and II, even in the presence of posterior infarction.

Pathologic Findings.—The heart weighed 679 grams and showed marked left ventricular hypertrophy. There was a completely healed infarct of the lower two-thirds of the anterior wall of the left ventricle. This infarct continued into the apical one-half of the lateral wall and extended through the left side of the septum and around the tip of the left ventricle to involve the

lower one-third of the posterior wall of the left ventricle and the posteroapical aspect of the right ventricle, as outlined in Fig. 2. In the anterolateral aspect of the apex, there was a large, partially calcified mural thrombus. The infarct occupied the subendocardial one-half to two-thirds of the anteroseptal and anterolateral walls and adequately accounted for the electrocardiographic pattern

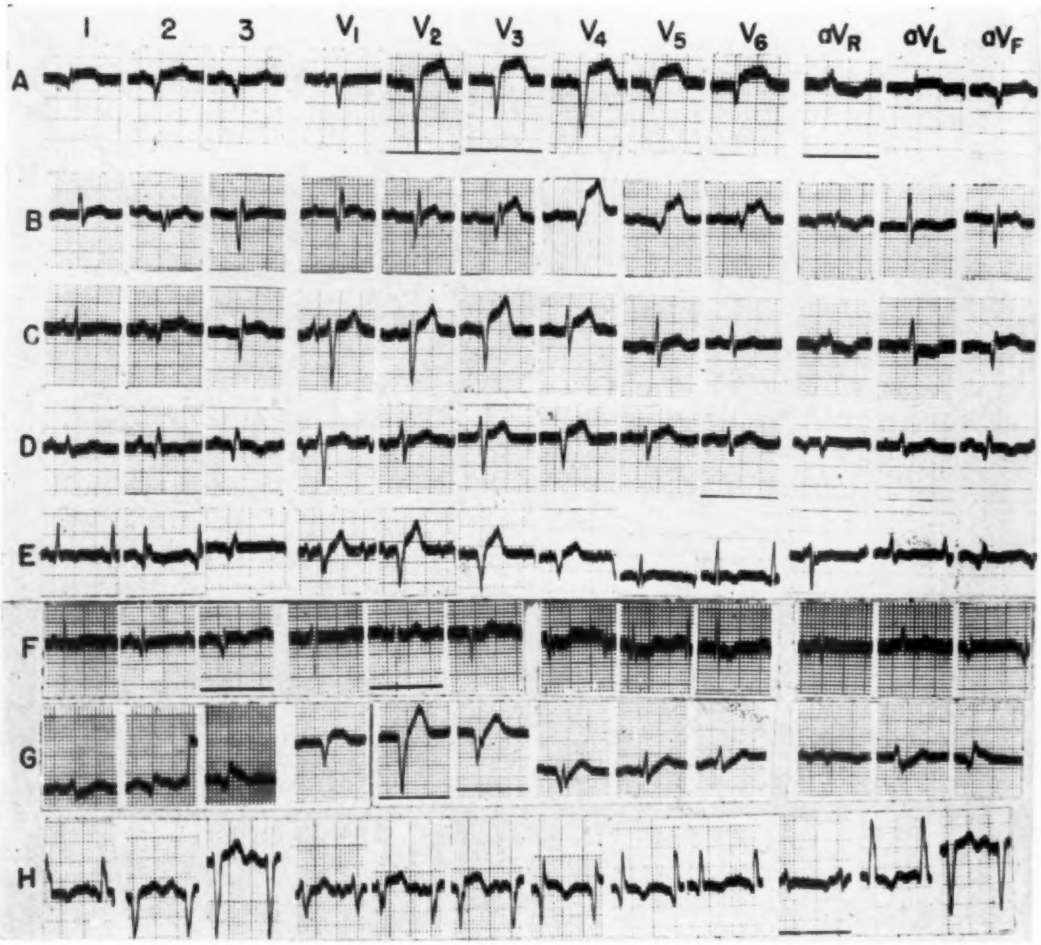

Fig. 3.—Recent anteroposterior infarction. Cases 53, 54, 55, 56, 57, 58, 59, and 60.

in Leads V_2 through V_5. In view of the extensive involvement of the lateral wall of the apex, an initial Q wave would have been anticipated in Leads V_6 and aV_L. Its disappearance in the former would suggest that the potential variations of the higher, uninfarcted part of the lateral wall had the predominant effect upon the recordings in these positions on Oct. 10, 1944. In view of the location of the infarct in the apical one-third of the posterior aspect of the left ventricle, the variable pattern in Leads aV_F, III, and II can be accounted for by changes in the electrical position of the heart with reference to the diaphragm. When the heart was in an intermediate position, the posteroapical aspect of the left ventricle probably rested upon the diaphragm and the infarction of the subendocardial two-thirds was presumably responsible for the abnormal Q wave.

When the heart dropped into a vertical position, a greater portion of the posterior aspect of the left ventricle probably came into contact with the diaphragm, including areas above the infarct. Transmission of potential variations from the epicardial surface of the uninfarcted basal two-thirds of the posterior wall may have been responsible for the initial R wave recorded on July 26, 1944.

CASE 53.—A 60-year-old diabetic woman was admitted in coma with right hemiplegia due to cerebral thrombosis. No cardiorespiratory symptoms were elicited after the patient regained consciousness. No cardiac glycosides were given. Death occurred on the twelfth hospital day.

Fig. 4.—Roentgenogram of injected heart in Case 53.

Electrocardiographic Findings.—An electrocardiogram made on the seventh hospital day is reproduced in Fig. 3, *A*. Leads V_2 through V_6 exhibited a QS complex, an abnormally high RS-T take-off, a straightening of the RS-T segment, and a monophasic, upright T wave typical of extensive anterior and anterolateral infarction in the stage of injury. Judging from the diphasic P wave in Lead V_1, the electrode was in the vicinity of the right atrium. The QS deflection in this lead suggested extension of the infarct into the septum. Lead aV_F showed a notched QS complex and a very slightly elevated RS-T junction which led to the diagnosis of extension of the infarct into the posterior aspect of the apex. In Lead aV_L there was a Q wave of 0.5 mm., an R wave of 2.5 mm., and T-wave changes typical of the stage of injury. The Q/R ratio in Lead I was much greater than that in Lead aV_L as a result of the positivity of the right arm. This made the pattern in Lead I characteristic of anterolateral infarction, whereas that in Leads II and III suggested posterior infarction.

Pathologic Findings.—The heart weighed 589 grams and exhibited a recent infarct of the anterior, lateral, and posterior aspects of the left apex and the intervening septum, as outlined in Fig. 4. The transmural infarction of the apical one-half of the anteroseptal wall adequately

explained the QS pattern in V_3 and V_4 and may have been partially responsible for the findings in Lead V_2. The infarction of the septum also may have contributed to the findings in Lead V_2 and was apparently responsible for those in Lead V_1. The lateral portion of the infarct was confined to the subendocardial two-thirds of the apical two segments and was not as extensive as would have been expected from the findings in Leads V_5 and V_6. However, a subsequent electrocardiogram, which is not reproduced, showed a QR complex in Leads V_5 and V_6 and thus corresponded more closely with the involvement of the lateral wall found at autopsy. The appearance of a late R wave in Leads V_5 and V_6 may have been due to recovery of the muscle in the subepicardial layer. A QS pattern was recorded in Lead aV_F on both occasions, despite the fact that the posterior portion of the infarct was confined to the apical one-third and was transmural in the apical segment only. If an infarct of such limited extent produced signs in Lead aV_F, it should have been manifested by a QR complex comparable to that recorded in Case 52. Two alternative explanations for the QS pattern in Lead aV_F were suggested by the findings in Leads aV_R and aV_L, which indicated that the heart was in a horizontal position with apex displaced backward. A horizontal position favors transmission of the potential variations of the right ventricle to the left leg and may lead to the registration of a QS complex in Lead aV_F as a normal variant or as a manifestation of septal infarction. The resemblance of the findings in Lead aV_F to those in Lead V_1 of this case was strongly in favor of a common origin. Backward displacement of the apex favors transmission of the potential variations of the anterior wall of the heart to the left leg, and would have led to a QS complex in Lead aV_F in this case, regardless of whether the dominant source came from the infarcted anterior wall of the left ventricle or from the anterior wall of the right ventricle, together with the infarcted septum. The fact that the RS-T pattern in Lead aV_F was more closely comparable with that in Lead V_1 than with that in Leads V_2, V_3, and V_4 favored a right over a left ventricular source.

CASE 54.—A 66-year-old woman was admitted to the hospital in profound shock with a history of repeated vomiting for two weeks and sudden onset of epigastric pain and weakness four days previously. No cardiac glycosides were given. Death occurred in circulatory collapse twenty-nine hours after admission.

Electrocardiographic Findings.—An electrocardiogram obtained ten hours before death is reproduced in Fig. 3, *B*. The QRS interval was 0.12 second. Leads V_1, V_2, and V_3 displayed a minute initial R wave 0.5 to 1.0 mm. in amplitude, followed by a larger S and R' deflection indicative of right bundle branch block. The contour of the RS-T segment and T wave in Leads V_1, V_2, and V_3 suggested that the right bundle branch block was the result of infarction of the septum. On the other hand, Leads V_1, V_2, and V_3 failed to show the QRS changes expected in leads over the right ventricle under these conditions. The initial upright deflection customarily recorded in right ventricular leads is derived from activation of the septum and is characteristically replaced by a Q wave when right bundle branch block is due to infarction of the septum. The slurred QS complex in Leads V_4 and V_5, together with the marked upward displacement of the RS-T junction, the upward concavity of the RS-T segment, and the monophasic, upright T wave were taken as evidence of complete transmural infarction of the anterior and anterolateral wall of the apex. The W-shaped QRS complex in Lead V_6, together with the marked RS-T displacement, indicated extension of the infarct well into the lateral wall of the left ventricle. On the other hand, Lead aV_L showed only a minute initial Q wave, followed by an RS complex and a very shallowly inverted T wave, and thus was not diagnostic of infarction. Close inspection of Lead aV_F revealed an RSR' complex much like that in Lead V_3 and suggested that the posterior inferior portion of the septum was in contact with the diaphragm and had the predominant effect upon the potential variations of the left leg. The standard leads were abnormal, but would have been difficult to interpret without reference to the precordial and unipolar extremity leads.

Pathologic Findings.—The heart weighed 416 grams and displayed a large recent infarct which involved the apical one-half of the anterior wall and the lower one-third of the lateral and posterior walls, like that in Case 53 (Fig. 4). This infarct extended through the entire thickness of the apical one-half of the interventricular septum and crossed over to involve the anterior wall of the right ventricle immediately adjacent to the septum. The recent transmural infarction of

the anterolateral wall adequately accounted for the findings in Leads V_4 and V_5, while the extension into the lateral wall explained the findings in Lead V_6. The abnormal RS-T pattern in Leads V_1, V_2, and V_3 could have been due to the lesion of the septum or to the lesion of the free wall of the right ventricle. If the right bundle branch block was due to the acute septal infarction, the initial R waves in Leads V_1, V_2, and V_3 were probably derived from activation of the uninfarcted upper half of the septum.

CASE 55.—A 75-year-old man was admitted to the hospital in profound circulatory collapse with a history of epigastric pain of four days' duration. Blood pressure was 70/60. A fairly loud systolic murmur was heard between the apex and lower end of the sternum and an indistinct diastolic murmur was made out in the same area. The patient was very cyanotic and remained in circulatory collapse, expiring thirty-three hours after admission.

Electrocardiographic Findings.—The electrocardiogram reproduced in Fig. 3, *C* was obtained seventeen hours after admission and following the administration of 4.0 c.c. of Digalen. A 2.0 mm. initial R wave was present in Leads V_1 and V_2 and was replaced by a slight slurring on the descending limb of the QS complex in Lead V_3. The last three precordial leads displayed an initial R wave which was 5.0 mm. tall in Lead V_4, 7.0 mm. in Lead V_5, and 5.0 mm. in Lead V_6. The localized QS pattern in Lead V_3 led to the diagnosis of a relatively small transmural infarct in the anteroseptal aspect of the left ventricle. The abnormal elevation of the RS-T junction in this lead indicated the presence of a recent infarct, but the concave upward curve of the RS-T segment was atypical. The 2.0 mm. elevation of the RS-T junction in Lead V_4 was abnormal and suggested extension of the infarct into the subepicardial aspect of the apex. Lead aV_F displayed a QR complex with an abnormally deep Q wave of 0.04 second duration, an elevated RS-T take-off, and a monophasic, upright T wave typical of recent posterior infarction. The RS-T segment showed reciprocal depression in Leads aV_L and aV_R which cancelled out in Lead I. The standard leads revealed no evidence of the lesion of the anterior wall, but were diagnostic of recent posterior infarction. Thus, the electrocardiogram gave definite evidence of coexistent anteroseptal and posterior infarct in the stage of injury.

Pathologic Findings.—The heart weighed 468 grams and showed a recent infarct which involved the anteroseptal and posterior one-half of the apex and intervening septum, as outlined in Fig. 5. The greatest extent of the infarct was in the interventricular septum, which was completely infarcted in the first four segments and perforated in the second and third segments. In view of the presence of a fairly characteristic murmur, it is probable that the septal perforation had occurred before the electrocardiogram was obtained. In spite of the extensive infarction and perforation of the septum, the QRS interval was only 0.09 second and normal initial R waves were present in Leads V_1 and V_2. These R waves probably were produced by activation of the outer wall of the right ventricle. The anteroseptal portion of the infarct was transmural in the apical two segments and was thought to be limited to the subendocardial two-thirds of the third segment; however, microscopic examination of the latter showed that the infarct reached the epicardium in this section, as well. The recent anteroseptal infarct accounted for the QS and RS-T displacement in Lead V_3 and was sufficiently large to have produced a similar pattern in Lead V_4. The R wave in this lead probably was derived from uninfarcted portions of the anterolateral wall beyond the boundary of the lesion. Transmission of positive potentials from more remote points would have been aided indirectly in this case by the fact that opposing cavity potentials available for transmission through the infarct to the overlying precordium were greatly reduced as a result of the extensive destruction of the septum and posterior wall.[24] Furthermore, the normal QRS pattern in Leads V_5 and V_6 corresponded with the absence of infarction of the lateral wall at autopsy. The posterior portion of the infarct was transmural in the apical two segments and subendocardial in the third segment and was thus clearly represented by the abnormal QR and RS-T displacement in Leads aV_F, II, and III.

CASE 56.—A 78-year-old man was well until six months before admission to the hospital, when he had an attack of prolonged, vise-like retrosternal pain and was treated by bed rest for three months. After resumption of activity, the patient had typical angina pectoris. About two weeks before admission, he had a second attack of prolonged retrosternal pain, following

which he was completely incapacitated because of orthopnea. While straining on a bed pan on the fifth hospital day, the patient suddenly expired.

Electrocardiographic Findings.—An electrocardiogram obtained on the second hospital day, after administration of 0.6 gram of digitalis, is reproduced in Fig. 3, *D*. An initial R wave was present in all precordial leads and measured 5.0 mm. in Leads V_1, V_2, and V_3, fell off to 1.0 mm. in Lead V_4, and increased to between 2.0 and 3.0 mm. in Leads V_5 and V_6. The sudden decrease in the amplitude of the initial R wave in Lead V_4 was abnormal and was attributed to a patchy infarction of the anterior wall near the apex. The 2.0 mm. elevation of the RS-T take-off and straightening of the segment with a monophasic, upright T wave in Lead V_4 suggested that the infarct was recent. Leads aV_F, II, and III showed an abnormal QR complex and cove-shaped inversion of the T wave, indicative of a posterior myocardial infarct which was probably in the stage of organization. Thus, from the electrocardiogram, the presence of an anteroposterior infarct, occupying much the same position as in the previous case, was postulated.

Fig. 5.—Roentgenogram of injected heart in Case 55, showing septal perforation in second and third segments.

Pathologic Findings.—The heart weighed 534 grams and exhibited (1) an old, healed transmural infarct of the apical one-half of the anterior wall, which extended through the septum and around the tip of the left ventricle to involve the apical two segments of the posterior wall, and (2) a recent posterior infarct, two to four weeks of age, superimposed upon the old lesion in the apical two segments and extending into the subendocardial one-half of the third and fourth segments, as outlined in Fig. 6. There was good correlation between the organizing posterior infarct and the QRS-T pattern in Leads aV_F, II, and III. On the other hand, there was poor correlation between the QRS pattern in the precordial leads and the large anterior infarct. There was complete replacement of the apical one-half of the anterior wall by fibrous tissue, resulting in a large aneurysm, but the only alteration in the QRS complex was an abnormal reduction in the amplitude

of the R wave in Leads V_4, V_5, and V_6. The question arises as to the source of the initial R wave recorded at precordial Positions 3, 4, and 5, which were apparently over the aneurysm. This R wave could scarcely have been produced by passage of the impulse through the aneurysmal wall. An initial R may be obtained over a complete transmural infarct in the presence of left bundle branch block, since activation of the septum from right to left causes early positivity of the left ventricular cavity and thus an initial R wave in all leads over the left ventricle. However, left bundle branch block can be excluded in this case by the QRS duration and the presence of a Q wave in Lead aV_F. The most likely source of the R wave in Leads V_4 and V_5 was the uninfarcted basilar one-half of the anterolateral wall. Because of the extensive posterior infarct, a consider-

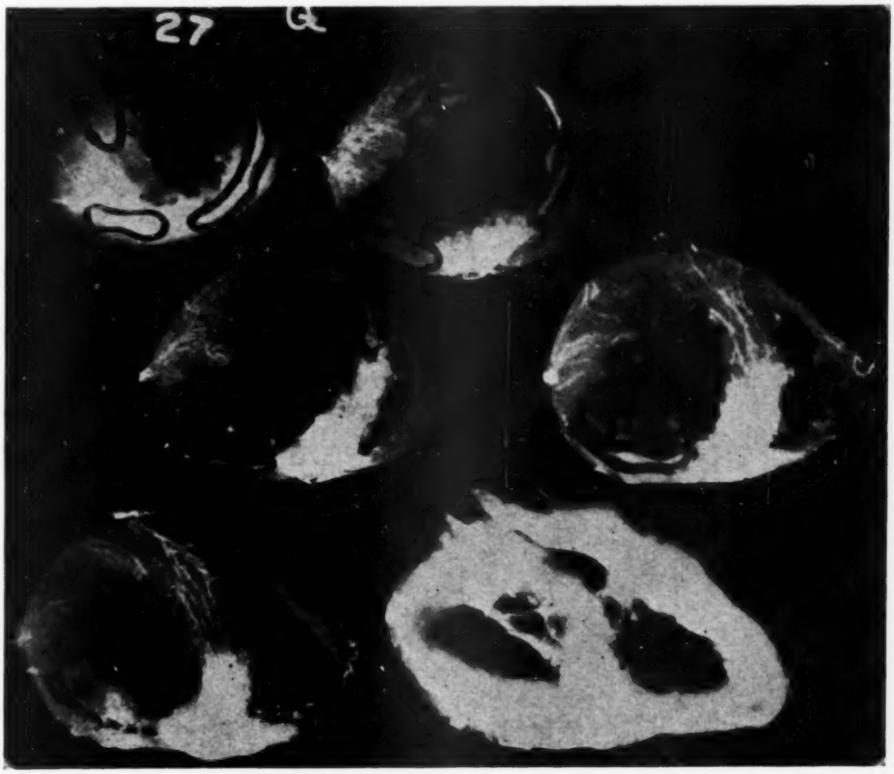

Fig. 6.—Roentgenogram of injected heart in Case 56, showing anteroposterior infarction and anteroapical aneurysm.

able reduction might have been expected in the negative potentials referred to the left ventricular cavity and available for transmission through the aneurysm to the precordium. This reduction in opposing forces may have indirectly facilitated transmission of positive potentials from the epicardial surface of the intact portions of the anterior wall to points on the precordium over the aneurysm. Abnormal RS-T elevation with a contour strongly suggestive of recent infarction, as in Lead V_4, is a common finding in leads over a cardiac aneurysm[24] and probably is representative of cavity potentials during repolarization. This case illustrates the alterations in the precordial lead pattern of anterior infarction which may result from an extensive coexistent posterior infarct.

CASE 57.—A 68-year-old man was well until six months prior to hospital admission, when he had a sudden attack of prolonged retrosternal oppression. He was treated at home by strict bed

rest for one week. After resumption of activity, he experienced typical angina pectoris. He was admitted in shock three days after the onset of a second attack of prolonged retrosternal pain and orthopnea. He failed to come out of the circulatory collapse and died thirty-four hours later.

Electrocardiographic Findings.—An electrocardiogram obtained nineteen hours after admission is reproduced in Fig. 3, *E*. In view of the distinct initial R wave in Lead V_1, the slurred QS complex in Leads V_2, V_3, and V_4 was indicative of infarction of the anteroseptal wall. The abnormally elevated RS-T junction and straightened RS-T segment and monophasic T wave were suggestive of recent infarction, but could have represented a fixed residue. Lead V_5 showed an abnormally broad Q wave which was 50 per cent of the amplitude of the succeeding R wave and thus was representative of extension of the infarct subendocardially into the anterolateral wall. The Q wave in Lead V_6 was too small to be of diagnostic significance, but the inverted T wave could have been an expression of a borderline ischemic zone. Lead aV_F displayed a QR complex typical of posterior infarction. This complex was characterized by a slurred Q wave measuring 0.03 second from onset to nadir, followed by a slurred, prolonged upstroke. The QRS interval amounted to 0.12 second in Lead aV_F and was distinctly longer than measurements in precordial leads. The coarse notching and broadening of the QRS complex in this lead indicated a conduction defect in the posterior wall of the left ventricle and was more in keeping with an old than with a recent posterior infarct. The findings in Lead aV_F were carried over into Leads II and III, so that the presence of posterior infarct could be readily recognized from the standard leads.

Pathologic Findings.—The heart weighed 420 grams and exhibited a recent infarct of the subendocardial one-half to two-thirds of the anterolateral wall, corresponding in position to the old anterior infarct in Case 59, represented by the broken lines of Fig. 7. In the apical segment this infarct extended through the septum and around the tip to the posterior aspect. Since the anterior infarct was not completely transmural, one would have expected a late positive potential in Leads V_2, V_3, and V_4 of greater magnitude than the small notch found in these leads. The marginal zonal pattern in Leads V_5 and V_6 corresponded satisfactorily with the extension of the recent anterior infarct into the subendocardial portion of the anterolateral aspect of the apex. In addition, there was an old, healed infarct of the subendocardial one-half of the posteroseptal wall which corresponded closely in position to the recent posterior infarct in Case 59 (Fig. 7). This accounted for both the abnormally broad and slurred Q and the broad, notched R wave in Leads aV_F, II, and III.

CASE 58.—A 68-year-old man gave a history of transient attacks of retrosternal oppression and dyspnea over a period of one year. The attacks were more frequent and severe during the week immediately preceding hospital admission. Hospital course was uneventful until the fourth day, when he experienced a sudden severe chest pain and died within a few minutes. No cardiac glycosides were given.

Electrocardiographic Findings.—An electrocardiogram obtained eight hours before death is reproduced in Fig. 3, *F*. The general resemblance of the QRS pattern to that in Case 57 (Fig. 3, *E*), will be noted. There was a small, but definite initial R wave in Leads V_1 and V_2, a narrow QS complex in Lead V_3, a W-shaped QS complex in Lead V_4, a triphasic QRS complex in Lead V_5 with Q/R ratio of 50 per cent, and a Q/R ratio of 20 per cent in Lead V_6. The findings in the precordial leads were diagnostic of anterolateral infarction. Lead aV_F showed a Q wave 0.03 second in duration and 2.0 to 3.0 mm. in depth, followed by an R wave 1.0 to 2.0 mm. tall. Except for the low voltage, these findings were diagnostic of posterior infarction. The RS-T junction in Lead aV_F was isoelectric, but the cove inversion of the T wave in this lead suggested a rather recent organizing posterior infarct. The marked depression of the RS-T junction and the straight downward slope of the segment in Leads V_4 through V_6 was not due to digitalis or allied drugs since none had been administered, either before or during hospitalization. The RS-T abnormalities could have been due to a recent infarct limited to the subendocardial layer of the anterolateral wall or could have been reciprocal to a recent posterior infarction. In the latter event, one would have expected elevation of the RS-T junction in Lead aV_F.

Pathologic Findings.—The heart weighed 444 grams and exhibited an old, partially calcified infarct involving the entire septum in the apical three segments and extending into the subendo-

cardial one-half of the anterolateral and posterior septal walls in these three segments. The distribution corresponded in general to that in Case 53 (Fig. 4), except in the third segment, where the infarct involved the entire septum and extended subendocardially into the posteroseptal wall. In the fourth segment there was a small area of anteroseptal infarction, almost identical with that of Fig. 4. Microscopic examination showed a recent transmural posteroapical infarct superimposed upon the old, healed subendocardial infarct. There was also recent reinfarction of the subendocardial one-third of the anterolateral wall. The anterolateral and posterior portions of the infarct found at autopsy corresponded with the electrocardiographic predictions. From the fact that the anterior infarct was not transmural, a better developed late R wave would have been anticipated in Leads V_3 and V_4. Despite the extensive infarct of the septum, an initial R wave was present in Leads V_1 and V_2 and probably was derived from activation of the outer wall of the right ventricle. The abnormal RS-T depression in Leads V_4, V_5, and V_6 may have been due either to the recent reinfarction of the subendocardial one-third of the anterolateral wall, to reciprocal effects of the recent transmural posterior infarct, or to a combination of the two.

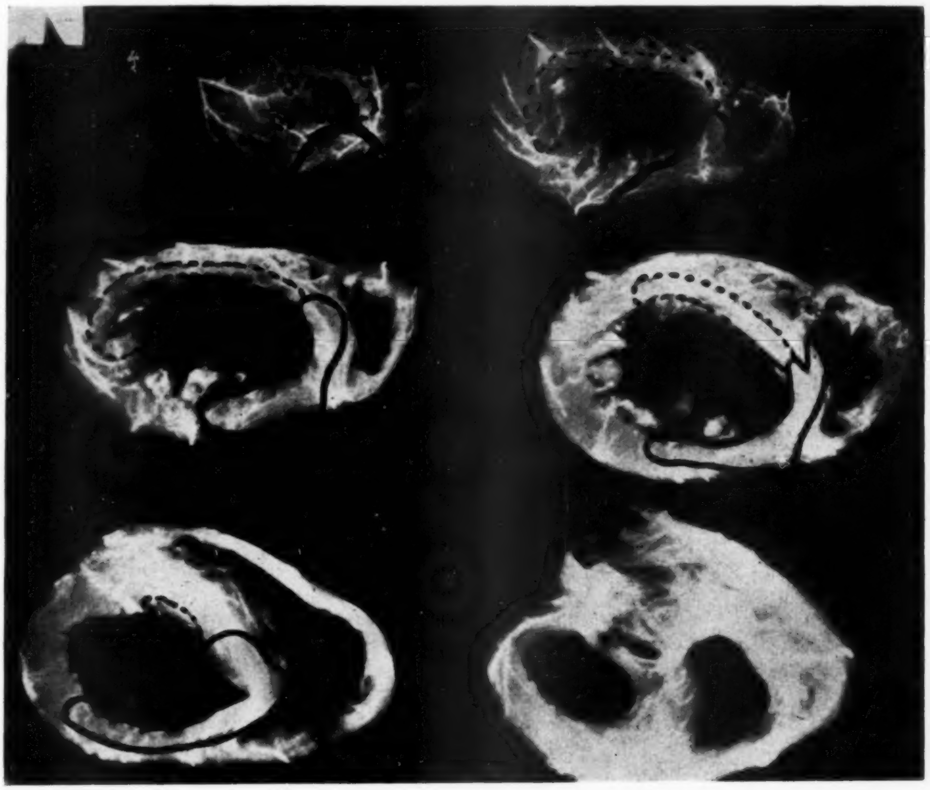

Fig. 7.—Roentgenogram of injected heart in Case 59 with recent posterior infarct demarcated by solid lines and old anterior infarct by broken lines.

CASE 59.—A previously healthy 51-year-old man was seized with sudden retrosternal burning pain and was admitted to the hospital in shock two hours later. Shortly after admission there was an episode of syncope during which no heart sounds were audible. An electrocardiogram taken as he recovered from the syncope showed ventricular tachycardia. This was stopped by quinidine, which was continued in doses of three grains every four hours for the remainder of his life. Death occurred on the fourth hospital day.

Electrocardiographic Findings.—An electrocardiogram obtained twenty hours before death is reproduced in Fig. 3, *G*. Attention is directed to the resemblance of the QRS pattern to that in Case 57 (Fig. 3, *E*). In Leads V_1 and V_2 a slurred QS complex was recorded; in Lead V_3 a QS complex with a late notch was present; and in Lead V_4 there was a W-shaped complex, upright component of which barely crossed the isoelectric line. In Leads V_5 and V_6 there was a triphasic QRS complex with a Q/R ratio of 25 per cent to 33 per cent. The findings in the last four precordial leads were indicative of an incomplete transmural anteroseptal infarct that extended subendocardially into the lateral wall of the left ventricle, whereas the findings in Leads V_1 and V_2 pointed toward extension into the septum. In Lead aV_F there was a broad, slurred Q wave which was 50 per cent of the succeeding notched R wave. The RS-T junction was abnormally elevated in Leads aV_F, II, and III and underwent changes indicating recent posterior infarction. The RS-T pattern in Leads V_3 through V_6 suggested that the anterolateral portion of the infarct was old, despite the negative past history.

Pathologic Findings.—The heart weighed 408 grams and exhibited a recent infarct of the posterior wall of the left ventricle and posterior one-half of the septum, together with an old, completely healed infarct of the subendocardial one-half of the anterolateral wall and anterior portion of the septum, as indicated by the solid and broken lines, respectively, in Fig. 7. The absence of the R wave from Leads V_1 and V_2 was probably the result of the extensive infarction of the septum. The question arose as to whether the conduction defect responsible for the prolongation of the QRS complex to 0.12 second was due to the lesion in the septum or to that in the outer wall of the left ventricle. When left bundle branch block is associated with extensive infarction of the septum, the left ventricular cavity may not become positive initially, because of failure of the septum to respond to the activating impulse. Although the combination of left bundle branch block with massive septal infarction is compatible with the registration of Q waves in left ventricular leads, it was probably not responsible for the conduction defect in this case, because it should have prolonged the QRS complex well beyond 0.12 second. The lesion in the free wall of the left ventricle could adequately explain both the QRS interval of 0.12 second and the QRS pattern in left ventricular leads. There was good correlation between the QRS-T pattern in Leads aV_F, II, and III and the recent posterior infarct. The old infarct of the anteroseptal wall was apparently responsible for the notched to W-shaped QS deflections in Leads V_3 and V_4. A larger late R wave should have been recorded in these leads because of the limitation of the anterior infarct to the subendocardial one-half of the wall, and because of the reduction in opposing forces due to the extensive posterior infarction. There was better correspondence between the QR pattern in Leads V_5 and V_6 and the extension of the infarct into the subendocardial portion of the lateral wall. Cases 57 and 59 were closely comparable, both as to QRS patterns and as to position of the anterior and posterior infarcts at autopsy. The RS-T segments and T waves pointed to a recent anterior and an old posterior infarct in the former and the reverse in the latter.

CASE 60.—A 64-year-old house-to-house salesman denied cardiac symptoms until two days before hospital admission, when he was seized with constrictive retrosternal pain which radiated down both arms and disappeared after a ten-minute rest. The pain returned in the evening, was accompanied by dyspnea, cough, and gross hemoptysis, and persisted until admission thirty-six hours later. Death occurred on the second hospital day. No cardiac glycosides were given.

Electrocardiographic Findings.—An electrocardiogram obtained three hours after admission and about thirty-six hours before death is reproduced in Fig. 3, *H*. The 3.0 mm. initial R wave of Lead V_1 decreased to 1.0 mm. in Lead V_2 and disappeared in Lead V_3, where it was replaced by a notched QS complex. In Lead V_4 there was a deep, broad Q wave and a relatively small late R wave. In Leads V_5 and V_6 there were Q/R ratios of 33 per cent and 20 per cent, respectively, but the Q wave was considered abnormal in both leads because of its slurring and the 0.04 second interval from its onset to nadir. The findings in the precordial leads were interpreted as evidence of a relatively large anterolateral infarct which was transmural in the anteroseptal region and subendocardial in the lateral wall of the apex. The classical RST-T pattern indicated that the infarct was recent. In Lead aV_L there was a 1.5 mm. Q wave which was only 12 per cent of the tall, slurred R wave of the same lead. These findings were transmitted from the left ven-

tricle and could have been due to uncomplicated left ventricular hypertrophy, but were also compatible with the presence of a small subendocardial infarct in a hypertrophied lateral wall. In Lead aV_F there was an initial Q wave 1.0 mm. deep, followed by a small R wave 1.0 mm. tall and then a deep, broad slurred S wave 13.0 mm. in amplitude. The small R and deep S waves were the reciprocal of the pattern in Lead aV_L and strongly suggested transmission of potential variations of the epicardial surface of the posteroinferior aspect of the right ventricle to the left leg. The unusual feature was the initial Q wave which preceded the small R wave. Although a QS complex may be recorded as a normal variant in leads from the right ventricle, an initial Q wave followed by an R wave and then an S wave represents an abnormal finding in these leads. Such a pattern may occur as a manifestation of infarction of the left side of the septum. The abnormal Q wave probably represented momentary initial negativity of the right ventricular cavity, as a result of onset of septal activation from right to left instead of in the usual direction. The small succeeding R wave may have been derived from subsequent activation of a portion of the septum by impulses distributed through the left Purkinje system or from passage of the impulse through the free wall of the right ventricle. Although analogy with the findings in left ventricular infarction might lead one to suspect the possibility of right ventricular infarction as the cause of the Q wave in Lead aV_F, leads facing the epicardial surface of an infarct involving the right ventricle, but not the septum, should display an initial R wave derived from activation of the septum in the usual fashion.

Pathologic Findings.—The heart weighed 530 grams and revealed a recent infarct of the apical one-third of the lateral wall which extended into the apical 1.0 cm. of the anteroseptal wall, as indicated by the solid lines of Fig. 8. This infarct was much smaller in size and more lateral in position than had been anticipated from the presence of a QS deflection in Lead V_3 and a deep Q and small R wave in Lead V_4, which was much more abnormal than the QR complexes in Leads V_5 and V_6. The marked degree of counterclockwise rotation suggested by the patterns in Leads aV_L and aV_F may have facilitated the transmission of the potential variations of the apical one-third of the lateral wall of the left ventricle to the precordium and thus may have accounted for the discrepancy in the position of the infarct, as predicted from the electrocardiogram and as found at autopsy. In addition, an old, healed subendocardial infarct was found in the posterolateral wall of the left ventricle, the posterior one-half of the septum, and the adjoining posterior wall of the right ventricle, as indicated by the broken lines in Fig. 8. By microscopic examination, this infarct was patchy in distribution and was practically confined to the subendocardial one-half of the free wall and the left half of the septum. The extension of this infarct into the posterior aspect of the septum was believed to be responsible for the abnormal initial Q wave which preceded the R and S deflections of Lead aV_F; the intact anterior one-half of the septum may have accounted for the initial R wave present in Leads V_1 and V_2.

CASE 61.—A 49-year-old man gave a typical history of angina pectoris for a period of two years. He was brought to the hospital in shock two hours after the onset of a very severe pain which had not been alleviated by ½ grain of morphine. Death occurred twenty-four hours later. No cardiac glycosides were given.

Electrocardiographic Findings.—An electrocardiogram obtained two and one-half hours after the onset of the present illness closely resembled that in Case 31.[24] A small initial R and a deep S wave were registered in Leads V_1 and V_2. QS deflections, upward displacement of the RS-T segments, and inversion of the terminal portion of the T waves were registered in Leads V_3 and V_4. An abnormal QR complex appeared in Leads V_5 and V_6. The precordial leads were thus diagnostic of a recent anterolateral infarction. The extremity leads were almost identical with those in Case 31, both in contour and voltage. The significant feature was a QR complex in both Leads aV_L and aV_F which pointed toward extension of the large anterior infarct into the subendocardial portion of the lateral and posterior aspects of the left apex.

Pathologic Findings.—The heart weighed 843 grams and shows marked left ventricular hypertrophy. There was a large recent infarct which involved the apical two-thirds of the anterior aspect of the left ventricle and extended through the septum and around the tip to the apical one-third of the lateral and posterior aspects, resembling that in Case 52 (Fig. 2). The infarct

was transmural in the apical one-half of the anterior wall of the left ventricle, but was confined to the subendocardial one-half of the lateral and posterior walls. From the microscopic sections, the infarct was estimated to be about twenty-four hours of age. Thus, there was good correlation between the electrocardiogram and autopsy findings in this case.

CASE 62.—A previously healthy 56-year-old man was seized with severe cramplike abdominal pain which began forty-five minutes after he had taken a cathartic and radiated to the precordium and ulnar aspect of the left arm and hand. The pain continued for the next twenty-four hours, accompanied by repeated vomiting, and led to admission on the surgical service because of the suspicion of an acute abdominal lesion. The hospital course was compatible with acute myocardial infarction, complicated by recurrent bouts of prolonged chest and shoulder pain. Death occurred suddenly on the thirty-eighth day. No cardiac glycosides were given.

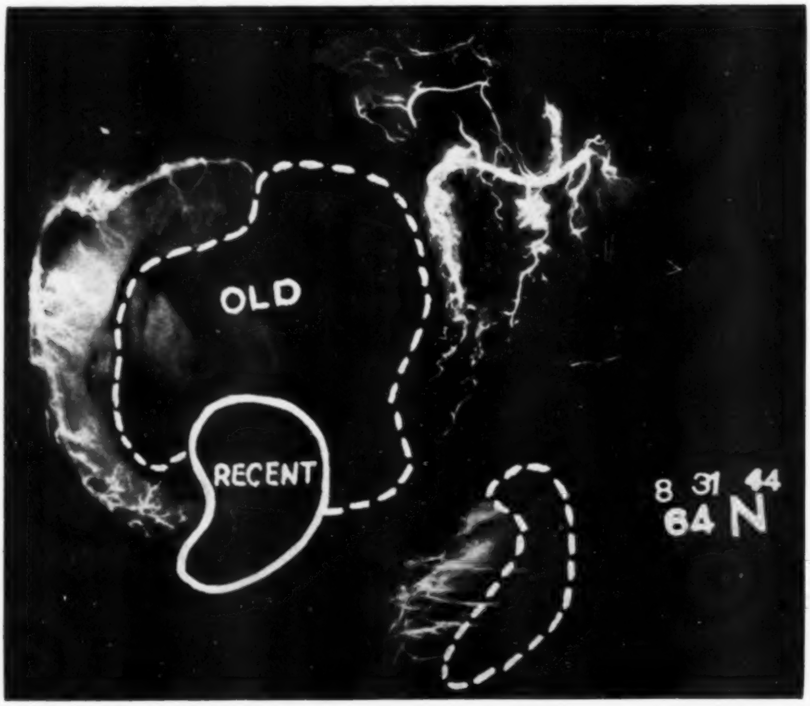

Fig. 8.—Roentgenogram of injected heart in Case 60 with recent anterolateral infarct indicated by solid lines and old posterior infarct by broken lines.

Electrocardiographic Findings.—An electrocardiogram (not shown) was first obtained on the fourth day and was repeated twice weekly thereafter. A minute initial R wave was intermittently present in Lead V_1 and a QS complex with a slurred descending limb was consistently found in Leads V_2 and V_3. A small R and deep S wave were recorded in Lead V_4 in the first tracing and a notched QS complex was registered in this lead in subsequent tracings. The RS-T segments and T waves in Leads V_2, V_3, and V_4 underwent an evolution typical of recent infarction. A diagnosis was consequently made of recent anteroseptal infarction. The QRS-T complexes in Leads V_5 and V_6 and Lead I of the first electrocardiogram were considered normal. Subsequently the initial R of Lead V_5 decreased to one-third of its original voltage and the T wave showed cove inversion. These changes were attributed to extension of the infarct into the subepicardial portion of the anterolateral wall. The QRS complexes in Leads V_6 and I showed no significant change,

but the T waves became inverted, presumably reflecting an outlying zone of ischemia. In Lead aV_L the QRS-T pattern was similar to that in Lead V_6, whereas in Lead aV_F a small R and deep S wave were recorded, presumably as a result of transmission of the potential variations of the posterior surface of the right ventricle to the left leg. The RS-T junction was elevated originally and the T wave sharply inverted in Leads aV_F, II, and III. The Goldberger leads were not repeated, but subsequent records of the standard leads showed no change in the RS pattern in Leads II and III, but a gradual return to an upright T wave of normal contour in the same leads. The original finding and subsequent evolution of the T waves were interpreted as evidence of transient ischemia of the posterior wall.

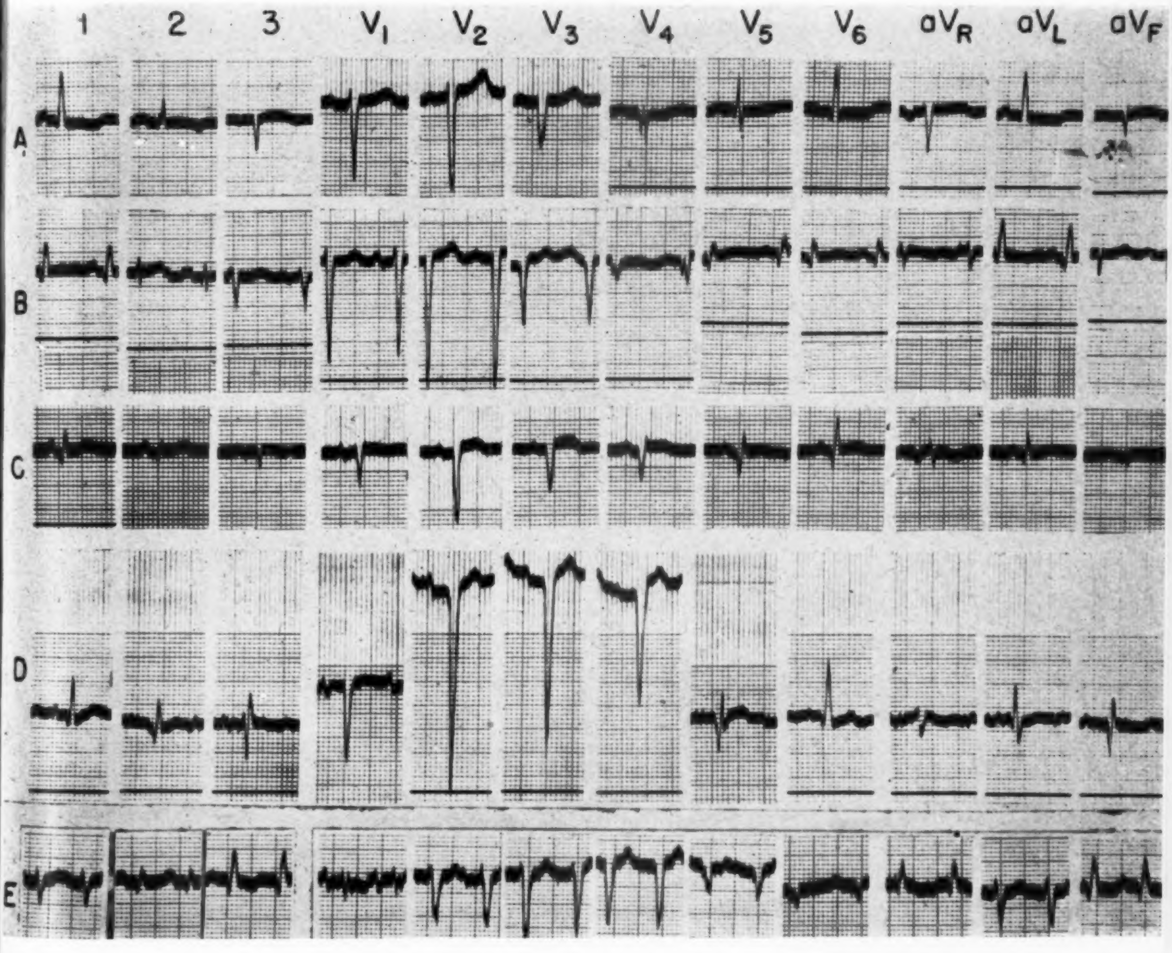

Fig. 9.—Old, healed anteroposterior infarction. Cases 63, 64, 65, 66, and 67.

Pathologic Findings.—The heart weighed 362 grams and exhibited an organizing infarct similar in distribution to that in Case 53 (Fig. 4). The infarct involved the apical two-thirds of the anteroseptal region and was in part transmural and in part patchy. It extended subendocardially into the apical one-third of the lateral and posterior aspects of the left ventricle. There was good correspondence between the findings in Leads V_2, V_3, and V_4 and the anteroseptal portion of the infarct. The involvement of the anterolateral wall at autopsy was more extensive

than had been anticipated from the electrocardiogram. Although the electrocardiographic findings suggested ischemia of the posterior wall, infarction was actually present. The absence of diagnostic QRS abnormalities in Lead aV_F was probably due to the horizontal position of the heart, with transmission of the potential variations of the posteroinferior wall of the right ventricle to the left leg.

CASE 63.—A 65-year-old diabetic man had had angina pectoris for several months, more frequent and more severe during the month prior to hospital entry. A classical history of myocardial infarction was not elicited. He was admitted in left ventricular failure, but soon became compensated and was practically asymptomatic during a period of six weeks of hospitalization and a subsequent follow-up for ten weeks in the out-patient department when he suddenly dropped dead.

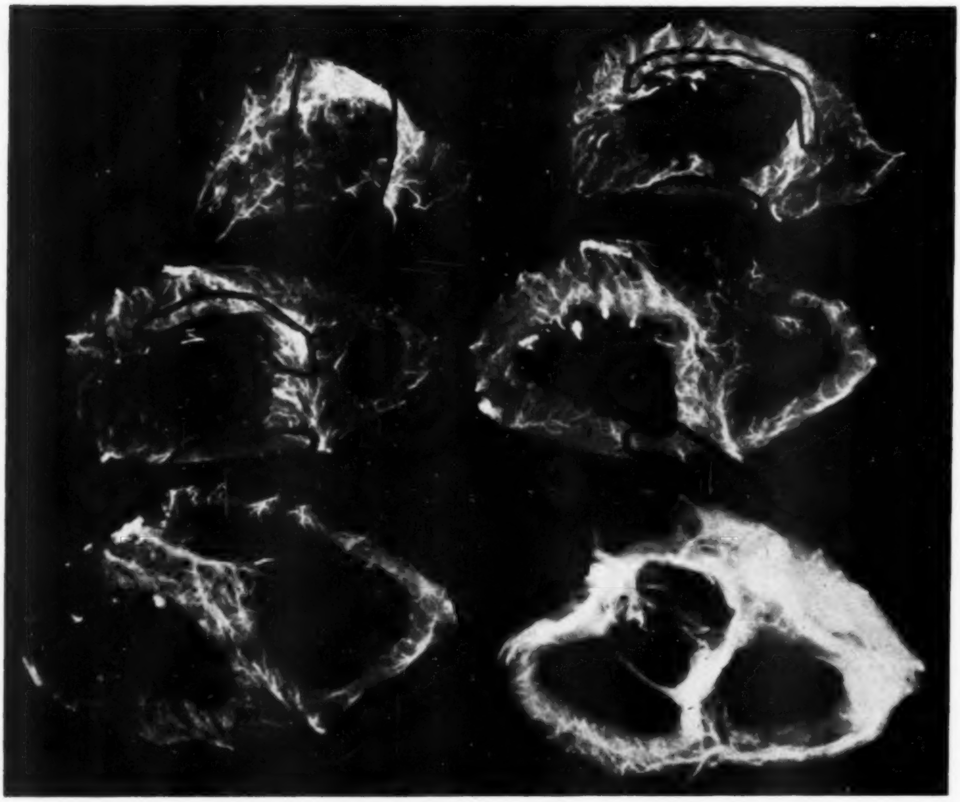

Fig. 10.—Roentgenogram of the injected heart in Case 63.

Electrocardiographic Findings.—An electrocardiogram obtained on the second hospital day, after the administration of 0.8 Gm. of digitalis, is reproduced in Fig. 9, *A*. Infarction of the anteroseptal aspect of the left apex was indicated by the slurred QS complex in Lead V_3 and the W-shaped complex in Lead V_4, taken in conjunction with the 2.0 to 3.0 mm. initial R wave in Leads V_1 and V_2. The T-wave pattern suggested that the infarct was old and this was borne out by the absence of significant serial changes over a period of six weeks. The lack of abnormal Q waves in Leads V_5, V_6, and aV_L suggested that the infarct had not extended significantly into the lateral wall. The deep, broad Q wave and small, late R wave of Lead aV_F indicated coexistent

posterior infarction and the dome-like RS-T segment raised the question of a more recent lesion. However, there were no significant changes in the RS-T segment and T wave of Leads aV_F, II, and III in serial tracings over a period of six weeks, so that it was finally concluded that the posterior infarction likewise was old and healed.

Pathologic Findings.—The heart weighed 520 grams and exhibited an old, healed anteroseptal infarct and a posteroseptal infarct which were continuous with one another around the tip of the left ventricle, as outlined in Fig. 10. The infarct was transmural in the posterior wall and at the apex, but was limited to the subendocardial one-third to one-half of the anteroseptal wall. The lateral wall had escaped, as predicted from the electrocardiogram. The autopsy findings confirmed the deductions drawn from Lead aV_F. In view of the subendocardial position of the anterior portion of the infarct, smaller Q and larger R waves would have been expected in Leads V_3 and V_4. The extension into the septum had produced no diagnostic changes in the electrocardiogram.

CASE 64.—An 80-year-old man had been in fairly good health until three months prior to hospital admission when he had had a typical attack of myocardial infarction, for which he was treated at home. After resumption of activity, there was progressive exertional dyspnea, followed by edema. The patient was admitted in advanced congestive heart failure and died two days later.

Electrocardiographic Findings.—An electrocardiogram taken on the first hospital day, after the administration of 0.2 Gm. of digitalis, is reproduced in Fig. 9, *B*. The findings in Leads V_1 through V_4 were comparable to those in the corresponding leads in Case 63. The decrease in the initial R wave between Leads V_1 and V_2, together with the presence of a notched QS complex in Lead V_3 and a W-shaped complex in Lead V_4, were diagnostic of infarction of the apical portion of the anteroseptal wall. On the other hand, the recordings in Leads V_5, V_6, and aV_L differed considerably from those in corresponding leads in Case 63. The abnormal QR pattern registered in these leads indicated that the infarct had extended subendocardially into the lateral aspect of the apex. There was intermittent variation in the QRS pattern in Lead aV_F, apparently of respiratory origin. Most cycles were characterized by a narrow QS deflection 3.0 to 5.0 mm. deep, but every fifth cycle consisted of a QR complex, the Q wave ranging from 25 per cent to 50 per cent of the amplitude of the R wave. The persistence of an abnormal Q/R ratio in Lead aV_F, in spite of respiratory variations in cardiac position, was strongly suggestive of posterior infarction. However, the findings in Lead aV_F could not be regarded as pathognomonic because of the brief duration of the Q wave. It is noteworthy that Lead III showed an initial R wave which corresponded to the reciprocal of the Q wave recorded in Lead aV_L. Thus, the posterior infarct was not revealed by the standard leads. The anterolateral infarct was suggested by the abnormal QR complex in Lead I. The contour of the T waves throughout the tracing pointed to an old, healed infarct.

Pathologic Findings.—The heart weighed 590 grams and exhibited an old, organized infarct of the anterior, lateral, and posterior aspects of the left apex, as outlined in Fig. 11. The anterior portion of the infarct involved chiefly the subendocardial one-half of the wall and, therefore, was not quite as extensive as anticipated from the notched QS complex of Leads V_3 and V_4. A dense organized infarct was found in the subendocardial three-fourths of the lateral wall in the apical segment, and patchy fibrosis was present in the portion of the lateral wall intervening between the two marked areas of infarction in the second and third segments. The electrocardiographic prediction of involvement of the lateral wall in this case, but not in Case 63, was borne out by the autopsy findings, but the extent of the lesion in the lateral wall was not quite as great as anticipated. Transmission of the potential variations of the transmurally infarcted posteroapical region to the left leg could account for the QS pattern, and shift in position to bring more of the posterobasal region into apposition with the diaphragm could account for the intermittent QR complex.

CASE 65.—A 44-year-old woman was hospitalized elsewhere ten months previously because of sudden left ventricular failure without accompanying pain. She was maintained on digitalis thereafter, but went into progressive congestive failure during the month prior to entry and was admitted with extreme anasarca. Death occurred on the fifth hospital day.

Electrocardiographic Findings.—An electrocardiogram obtained on the first hospital day is reproduced in Fig. 9, *C*. The QS complex in Lead V_3 and the QR complex in Lead V_4 were indicative of incomplete transmural anteroseptal infarction; the abnormal QR pattern in Leads V_5, V_6, and aV_L signified extension subendocardially into the lateral wall; and the QS complex, as in Leads V_1 and V_2, suggested continuation into the septum. The W-shaped QRS pattern in Lead aV_F was suggestive of coexistent posterior infarction, but the voltage was too low for the finding to be diagnostic. The presence of a prominent Q wave in all three standard leads pointed to anteroposterior infarction. In another tracing, taken two days later, the heart had shifted from a semi-horizontal to a vertical position. Lead aV_L showed a 0.5 mm. initial R wave and a 3.0 mm. S wave, presumably transmitted from the epicardial surface of the right ventricle. Lead aV_F showed a Q wave of 1.0 mm. and an R wave of 3.5 mm., which was still suggestive of posterior infarction. The standard leads showed right axis deviation and, like Lead aV_L, no longer revealed evidence of the lateral infarction. Because of the contour of the T waves in the original tracing and the absence of change in the precordial leads, it was concluded that the infarct was old and healed.

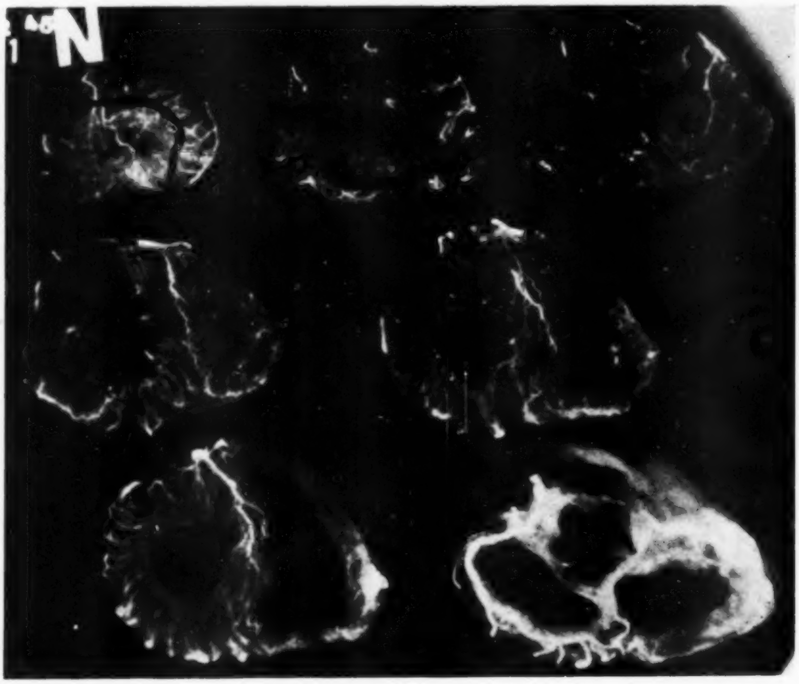

Fig. 11.—Roentgenogram of the injected heart in Case 64.

Pathologic Findings.—The heart weighed 480 grams and exhibited a completely healed infarct which involved the anterior, lateral, posterior, and septal walls of the left ventricle in the apical two segments and the anterior and septal aspects in the next three segments, as depicted in Fig. 12. Because of the moderate right ventricular dilatation found at autopsy, it is probable that the potential variations of the right ventricle and right side of the septum were referred to precordial Position 3 as well as to Positions 2 and 1. If the electrode at Position 3 were over the anterior wall of the right ventricle, the QS complex recorded in this lead could be correlated with the extensive infarction of the septum. On the other hand, if the electrode at Position 3 had been over the mid-portion of the anteroseptal wall of the left ventricle, one would have expected a QR complex more like that registered at Positions 4 and 5, inasmuch as the infarct of the anteroseptal

portion of the outer wall was subendocardial in location. The QR complex in Leads V_4, V_5, V_6, and aV_L conformed closely with the infarction of the subendocardial portion of the anterior and lateral aspects of the left apex. The infarction of the posteroapical aspect of the left ventricle could have been responsible for the QR pattern recorded in Lead aV_F in the second electrocardiogram, but did not seem sufficiently extensive to have explained adequately the W-shaped QS complex recorded in the tracing reproduced in Fig. 9, *C*.

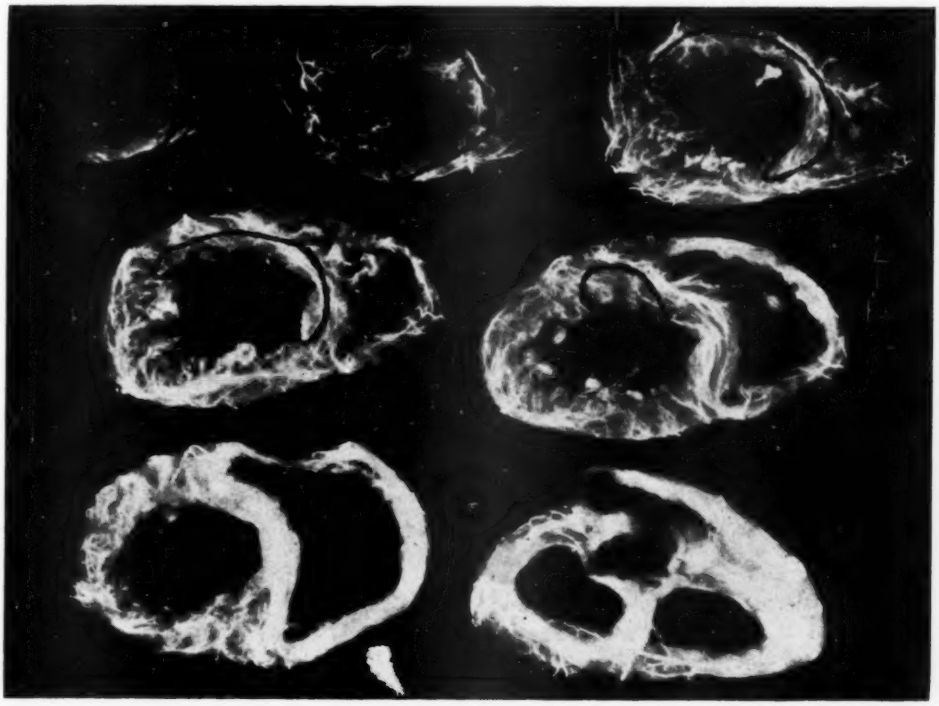

Fig. 12.—Roentgenogram of the injected heart in Case 65.

CASE 66.—A 62-year-old man gave a history of a single attack of prolonged, stabbing precordial pain, followed by congestive heart failure, five years previously. The patient made an excellent recovery and was symptom free until the day of admission when he was seized suddenly with sharp periumbilical pain, followed by nausea and vomiting. There were physical findings of mesenteric thrombosis, which caused death four days later.

Electrocardiographic Findings.—An electrocardiogram obtained after the administration of 1.6 mg. of Cedilanid and four hours before death is reproduced in Fig. 9, *D*. Lead V_1 displayed a small, but distinct Q wave 0.5 mm. in depth, a slightly larger R wave, and a deep S wave 16.0 mm. in amplitude. The Q wave preceding the RS complex in V_1 was abnormal and was attributable to infarction of the septum. The R wave was probably derived from activation of the free wall of the right ventricle. Lead V_2 showed a deep QS complex, with a notch near the base of the descending limb which was probably the counterpart of the R wave of Lead V_1. The abnormalities in Lead V_2 were attributed also to infarction of the septum. A deep QS complex with smooth limbs was recorded in Leads V_3 and V_4 and was interpreted as evidence of transmural infarction of the free portion of the anteroseptal wall. Lead V_5 displayed a deep, slurred Q wave, followed by R and S waves. Lead V_6 showed a small, but abnormally broad, slurred Q wave. The findings in Leads V_5 and V_6 were attributed to extension of the infarct subendocardially into the lateral wall of the left ventricle. The contour of the RS-T segments and T waves was more in keeping with old,

healed infarction. In Lead aV_F there was an initial R wave 0.5 mm. in height, an S wave 6.0 mm. in depth, and an R′ 5.0 mm. tall. The last two phases of the QRS complex in Lead aV_F were suggestive of posterior infarction, but the presence of an initial R wave prevented an unqualified diagnosis. A broad, slurred or notched Q wave was registered in Leads I and II. Reference to the unipolar limb leads showed that this Q wave was due, in large part, to initial positivity of the right arm.

Pathologic Findings.—The heart weighed 660 grams and exhibited a completely healed, sheet-like subendocardial infarct involving the entire posterior wall, the apical two-thirds of the anteroseptal wall, and the apical one-third of the lateral wall. The anterior and posterior infarcts were continuous through the septum and around the tip of the ventricle, but were confined largely to the subendocardial one-fourth of the wall. The QRS pattern in Leads V_1 and V_2 was well correlated with the infarction of the left side of the septum. However, the smooth QS complexes in Leads V_3 and V_4 could scarcely have been produced by infarction limited to the subendocardial one-fourth of the free portion of the anteroseptal wall. In view of the autopsy findings, it is probable that precordial Positions 3 and 4 also lay just to the right of the infarcted septum or over it. The QS pattern was thus referable to the septal lesion and the QR deflection of Leads V_5, V_6, and aV_L was attributable to the infarction of the subendocardial portion of the anterolateral wall. The RSR′ complex of Lead aV_F was apparently a manifestation of the posterior portion of the infarct. The initial R wave was probably derived from intact islands of muscle in the subendocardial layer.

CASE 67.—A 50-year-old man was well until six months before hospital admission, when he had an attack of prolonged, stabbing precordial pain, followed by left ventricular failure. During the twelve days prior to entry, he had two attacks of sudden, boring epigastric pain, accompanied by dyspnea. He was admitted in severe congestive failure, but responded satisfactorily until the ninth hospital day when there was a third attack of sudden epigastric pain, accompanied by orthopnea, cyanosis, and shock and followed by jaundice. Signs of phlebothrombosis were discovered in the calves of the legs. Further attacks occurred on the fifteenth and seventeenth days, the latter ending fatally.

Electrocardiographic Findings.—An electrocardiogram obtained on the second hospital day, after the administration of 0.8 Gm. of digitalis, is reproduced in Fig. 9, *E*. A preliminary survey of the precordial and unipolar limb leads pointed to a marked clockwise rotation on both the longitudinal and anteroposterior axes, coupled with backward displacement of the apex, so that the potential variations of the right ventricle were transmitted to a larger portion of the precordium and to the left arm, those of the posteroapical aspect of the left ventricle to the left leg, and those of the posterobasal aspect of the left ventricle to the right arm. The RSR′ complex recorded in Leads V_{3R} and V_1 raised the question of incomplete right bundle branch block, but the low voltage and the apparent coincidence of this R′ deflection with the late R wave of Lead aV_R suggested that the R′ was of left ventricular origin. The pattern in the standard leads also suggested right bundle branch block, but if the interpretation of the Goldberger leads was correct, the broad, slurred S wave of Lead I and R wave of Lead III were actually of left ventricular origin. An initial R wave, within normal limits, was found in Leads V_1, V_2, and V_3; a barely detectable initial R wave was made out in Lead V_4, and a broad, notched or slurred QS complex was recorded in Leads V_5 and V_6. At first glance, these findings suggested infarction of the lateral aspect of the apex, but in view of the marked clockwise rotation, they could have resulted from infarction localized to the anteroseptal aspect of the apex. From the 0.03 second duration of the Q wave in Lead aV_F, the Q/R ratio of 40 per cent, and the abnormally late attainment of the peak of the R wave, it was thought that the infarct extended into the subendocardial portion of the posteroapical wall. A second tracing on the eleventh hospital day showed no significant change in the QRS-T pattern, in spite of a history of pulmonary embolism two days previously. Unfortunately, the electrocardiogram was not repeated after the fourth and fifth attacks.

Pathologic Findings.—There were several pulmonary emboli of different ages, and a large terminal embolus was the immediate cause of death. The heart weighed 590 grams and exhibited left ventricular hypertrophy, acute right ventricular dilatation, and an old, healed anteroposterior

infarction, as outlined in Fig. 13. There was dense infarction of the subendocardial two-thirds of the anterior wall in the two apical segments and patchy infarction of the subepicardial one-third. The infarct extended around the tip of the ventricle and through the septum to involve the subendocardial one-half, or mid-zone, of the posterior wall from apex to base. There was satisfactory correlation between the pattern in Lead aV_F and the thickness of the posterior infarct. The fact that the greater part of the lateral wall had escaped infarction is noteworthy, in view of the QS pattern in Leads V_5 and V_6. It is probable that the clockwise rotation of the heart (produced by the demonstrated right ventricular dilatation and lowering of the diaphragm) carried the infarcted anteroapical wall of the left ventricle into a position which facilitated transmission of the potential variations of its epicardial surface into the axilla. The very minute R wave in Lead V_4 was probably a manifestation of the anteroseptal infarct. Despite repeated pulmonary emboli, the T waves did not become inverted in precordial leads over the right ventricle.

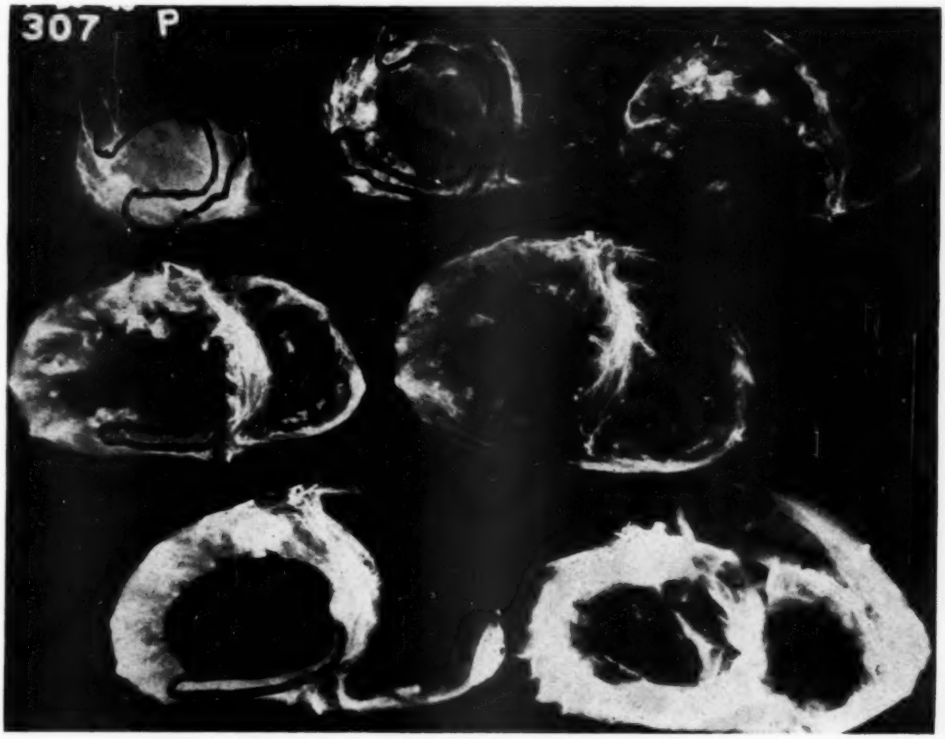

Fig. 13.—Roentgenogram of the injected heart in Case 67.

Case 68.—A 53-year-old man gave a history of repeated episodes of congestive failure over a period of two years, during the course of which he was treated in other hospitals on five different occasions. There was no definite history of myocardial infarction. He was admitted in severe congestive failure and died on the twenty-eighth hospital day.

Electrocardiographic Findings.—Electrocardiograms were obtained at intervals of ten days during hospitalization, but are not reproduced because of the close resemblance to that in Case 67 (Fig. 9, *E*). A rather small R wave and deep S wave were present in Leads V_1, V_2, and V_3, a slurred QS complex in Lead V_4, and a notched QS complex of relatively low voltage in Leads V_5 and V_6. The T waves in Leads V_2, V_3, and V_4 were almost identical with those in Case 67, and those in Leads V_5 and V_6 were low and upright. These findings were indicative of an old, healed anterolateral infarct. Lead aV_F revealed a QR complex similar in duration and contour to that

in Case 67, but low in voltage. This QR pattern was strongly suggestive of continuation of the infarct into the posterior wall, but could not be regarded as pathognomonic because of the low voltage.

Pathologic Findings.—The heart weighed 816 grams and exhibited marked left ventricular hypertrophy and secondary right ventricular dilatation and hypertrophy. There was an old transmural anterior infarct in the apical two segments and a mid-zonal anterior infarct in the third segment, corresponding closely to the distribution of the anterior portion of the infarct in Case 67 (Fig. 13), except for lack of penetration of the septum. There was a separate infarct of the posterior wall in the apical four segments, corresponding approximately to the distribution of the posterior infarct in the first four segments in Case 67. The posterior infarct involved the subendocardial one-half except in one area where it was transmural. Since practically all of the lateral wall escaped infarction, it is probable that the notched QS pattern in Leads V_5 and V_6 was due to transmission of the potential variations of the transmurally infarcted anterior apical wall to the axilla consequent upon marked clockwise rotation of the heart, comparable to the situation discussed in more detail for Case 67.

COMMENT

The purpose of the present study is to determine the reliability of multiple precordial and unipolar limb leads in the detection of anteroposterior infarction and to evaluate the effects of coexistent posterior infarction on the electrocardiographic signs referable to the anterior lesion, and vice versa.

The term "anterior infarction," when used without further qualification, included small lesions localized to the apical one-third or more of the anteroseptal or anterolateral wall and large lesions covering both aspects. The criteria utilized for an appraisal of the findings referable to the anterior portion of the lesion in each individual case were established through previous studies in which the findings in multiple precordial leads were correlated with the distribution of the infarct in the anteroseptal[27] and anterolateral[24] walls. The problem thus resolved itself into (1) the decision as to whether the abnormalities in the precordial leads conformed with, exceeded, or fell significantly short of expectations based on the size and position of the anterior lesion at autopsy; and (2) the decision as to whether significant discrepancies were secondary to or independent of the coexistent posterior infarction.

The term "posterior infarction," when used without further qualification, included all lesions occupying the apical one-third or more of the posterior wall. An attempt was made to classify the findings in Lead aV_F as negative, suggestive, or diagnostic of posterior infarction and to determine whether the diagnostic failures were attributable to the coexistent anterior infarction or to other causes.

The criteria for the evaluation of the findings in Lead aV_F will be discussed in detail in a forthcoming communication on posterior infarction, but are summarized briefly at this time for reference purposes. QR complexes of 0.5 mv. or more were considered diagnostic of posterior infarction when the Q wave measured 0.03 second or more from onset to nadir and exceeded 25 per cent of the amplitude of the associated R wave, and were classed as borderline to strongly suggestive when they met one of these two requirements. QR deflections of low voltage, which conformed with the foregoing criteria, were regarded as strongly suggestive of posterior infarction, but when the duration of the

Q wave was 0.04 second or more, they were classed as definitely abnormal. QR complexes of 0.5 millivolt or more in Lead aV_F, characterized by a distinct Q followed by a coarsely slurred or notched prolonged upstroke, were regarded as a manifestation of old posterior infarction, even though the duration of the Q wave or the Q/R ratio did not meet the foregoing minimal requirements. QS deflections of 0.5 mv. or more, which consumed 0.03 second or more from onset to nadir, were attributed to posterior infarction, provided that there was evidence to indicate that the potential variations of the left leg were derived principally from the posterior wall of the left, rather than the right ventricle.

The cases have been classified into three main groups on the basis of the pathologic findings: (1) those with recent, anatomically continuous anteroposterior infarction; (2) those with healed, confluent anteroposterior infarction; and (3) those with two or more separate lesions. Further subdivision has been made according to the size of the posterior infarct.

Correlation of Electrocardiographic and Pathologic Findings in Recent Anteroposterior Apical Infarction.—In twenty cases autopsy revealed a recent infarction of the apical one-half or more of the anterior wall of the left ventricle, the infarction continuing through the septum and around the tip to involve the apical one-third or more of the posterior wall of the left ventricle. The anterior and posterior lesions were regarded as uniform in age in all but one case (Case 20), in which they were separated by an interval of four days. Thus, the pathologic findings in the other nineteen cases were indicative of a single, simultaneous infarction of the anterior and posterior aspects of the apex. The cases were further subdivided into two groups in accordance with the extent of involvement of the posterior wall: (a) fifteen cases in which infarction was confined to the apical one-third of the posterior wall (Cases 26, 27, 29, 30, 31, 34, 37, 41, 42, 53, 54, 61, 62, 69, and 80); and (b) five cases in which infarction involved the apical one-half or more of the posterior wall (Cases 20, 55, 58, 71, and 81).

A review of the electrocardiograms of the fifteen cases in which the posterior part of the infarct was limited to the apical one-third showed that the findings in the precordial leads did not differ significantly from those in cases with a comparable anterior infarct, but without involvement of the posterior wall. The precordial leads revealed abnormal Q-wave patterns diagnostic of anterior infarction in fourteen of the cases, but showed minute initial R waves in one (Case 34), apparently as a result of early positivity of the left ventricular cavity secondary to an almost complete infarction of the left side of the septum.[24]

On the other hand, Lead aV_F proved very disappointing for the detection of extensions confined to the apical one-third of the posterior wall. A QR complex was recorded in this lead in only three of the fifteen cases (Cases 31, 61, and 69). The voltage was low in each instance, but the findings were considered definitely abnormal in Case 69 because of a Q-wave duration of 0.04 second. The Q/R ratio was high in the other two cases, but the findings were classed as borderline in view of a Q-wave duration below 0.03 second. A QS deflection was recorded in Lead aV_F and all precordial leads in Case 53 and led to an ante-mortem diagnosis of extensive transmural infarction of the posterior, as well as the anterolateral wall. However, at autopsy the posterior part of the infarct was confined to

the apical one-third and was transmural in the apical segment only. From experience with other cases, it seemed improbable that so small a lesion was responsible for the QS pattern in Lead aV_F. Since the heart was in the horizontal position with backward displacement of the apex, the potential variations of the left leg were probably transmitted from the right ventricle or perhaps in part from the anterior wall of the left ventricle. In the former event, the QS complex in Lead aV_F could have been a manifestation of the extensive infarction of the septum, and in the latter event, it could have been a manifestation of the extensive transmural anterior infarct.

Lead aV_F yielded no signs which could even justify a suspicion of posterior infarction in the remaining eleven cases. Relatively small R and deep S waves were recorded in eight of these eleven cases and were attributed to the predominant transmission of the potential variations of the posteroinferior wall of the right ventricle to the leg, secondary to horizontal position. In two of the patients with posteroapical infarction (Cases 26 and 37), the heart was in the intermediate position, and in a third patient (Case 42), it shifted from a semihorizontal to an intermediate position. Under these circumstances, the potential variations of the posterior wall of the left ventricle were transmitted to the left leg and were manifested by a large initial R wave in Lead aV_F in the two former and a small monophasic upright deflection in the latter. The absence of a Q wave was noteworthy in all three cases, but particularly in Case 26, where there was pathologic evidence of transmural infarction of the entire apical one-third of the posterior wall. Two factors were probably responsible for the absence of an initial downward deflection in Lead aV_F: (1) derivation of the potential variations of the left leg, chiefly from those of the intact basal two-thirds of the posterior wall of the left ventricle; and (2) marked reduction in the opposing negative cavity potentials available for transmission through the infarcted apical one-third of the posterior wall, as a result of the extensive lesion of the anterior wall and septum.

In addition to the five cases of recent anteroposterior infarction, which involved the apical one-half or more of the posterior wall, there were four other cases of recent anteroposterior apical infarction complicated by a separate lesion of the basal portion of the posterior wall (Cases 35, 38, 57, and 74), one case of old anteroposterior infarction complicated by recent massive posterior infarction (Case 56), and one case of healed anteroposterior infarction in which serial tracings were obtained during the acute stage (Case 19). These eleven cases have been analyzed in a group to bring out the electrocardiographic findings of an extensive anterior infarct in the presence of an extensive posterior infarct, and vice versa.

Abnormal Q-wave patterns in the precordial leads, commensurate with the extent of the involvement of the anterior wall at autopsy, were found in only five of the eleven cases (Cases 20, 57, 58, 71, and 74). The absence of Q waves from the precordial leads was attributable to the earliness of the lesion in Case 38 and to initial positivity of the left ventricular cavity secondary to a septal lesion

in Case 81. Typical signs of anteroseptal infarction were originally present in Case 19 and were obliterated at the development of an extensive posterior infarction two weeks later. The absence of Q waves from the precordial leads in Cases 35 and 56 and their limitation to only one lead in Case 55 was probably in part a secondary manifestation of the extensive posterior infarct and attributable to reduction in the opposing negative cavity potentials available for transmission through the anterior wall.

With respect to the findings in Lead aV_F, the group in which there was anteroposterior infarction with extensive involvement of the posterior wall contrasted sharply with the group in which the lesion was confined to the apical one-third of the posterior wall. Lead aV_F displayed signs which were regarded as diagnostic of posterior infarction in seven cases (Cases 20, 38, 55, 56, 57, 58, and 71). The findings were diagnostic of posterior infarction during the acute stage in another case (Case 19), but became borderline after the lesion healed. The pattern in Lead aV_F in Case 81 was somewhat suggestive of posterior infarction, but was difficult to interpret because of the extremely low voltage of the QRS complex. Broad, slurred Q and notched R waves, which fulfilled the criteria for a diagnosis of posterior infarction, were also recorded in Lead aV_F in Case 74. However, the QR pattern and the time of onset of the intrinsicoid deflection in Lead aV_F corresponded closely with that in Lead V_1. The findings in the precordial leads were typical of right bundle branch block as a result of infarction of the septum and anterior wall and corresponded closely with the lesion found in these structures at autopsy. Although posterior infarction also was demonstrated at autopsy, the findings in Lead aV_F were due to the septal rather than the posterior lesion. Reference of potential variations of a septal infarct to the left leg to produce signs simulating posterior infarction was facilitated by horizontal position of the heart, made evident in this case not only by the resemblance of Lead aV_F to V_1, but also by the resemblance of Lead aV_L to V_6. A similar pattern would have been recorded in Lead aV_F as a result of septal infarction in a horizontally placed heart, even though the posterior wall of the left ventricle were intact. Under these circumstances, a mistaken diagnosis of posterior infarction would have been made unless the findings in the unipolar limb leads were interpreted in the light of those in the precordial leads. The more common effect of horizontal position is to interfere with the registration of signs of a posterior infarction in Lead aV_F, as exemplified by eight of the fifteen cases in the previous group and one of the eleven cases in the present group (Case 35).

Correlation of Electrocardiographic and Pathologic Findings in Old Anteroposterior Apical Infarction.—Sixteen cases were observed with old healed infarction of the apical one-third or more of the anterior wall of the left ventricle, which was continuous through the septum and around the tip of the ventricle with an old healed infarct of the apical one-third or more of the posterior wall. The findings at autopsy were compatible with a single lesion in all cases, but were actually due to confluence of separate anterior and posterior infarcts in at least

two cases (Cases 19 and 86), as shown by serial electrocardiograms. The findings in Case 19 have been discussed, for serial electrocardiograms were obtained during the acute stage. The original tracings in Case 86 showed localized posterior infarction, and subsequent tracings eighteen months later revealed right bundle branch block due to a complicating septal infarction.

The QRS pattern in the precordial leads of these fifteen cases corresponded satisfactorily with the involvement of the anterior wall at autopsy. For correlation of electrocardiographic and pathologic findings referable to the healed lesion of the posterior wall, the cases were further subdivided into two groups: (a) seven cases with infarction confined to the apical one-third of the posterior wall (Cases 18, 47, 48, 50, 52, 65, and 153); and (b) eight cases with infarction involving the apical one-half or more (Cases 51, 63, 64, 66, 67, 86, 96, and 152).

The findings in Lead aV_F were negative in four of the seven cases of the former group, suggestive of posterior infarction in one (Case 65), barely diagnostic in one (Case 47), and intermittently diagnostic in one (Case 52). In the latter case the findings were subject to considerable postural variation and were characterized by an abnormal QR complex when the heart was in intermediate position and by a coarsely notched monophasic upright deflection when the heart shifted into vertical position. Intermediate position probably favored transmission of the potential variations of the infarcted apical one-third of the posterior wall to the left leg, resulting in the registration of an abnormal Q wave, whereas vertical position probably favored transmission of the potential variations of the intact basal two-thirds, resulting in the replacement of the Q wave by a coarse notch near the base of the ascending limb of the R wave. Semivertical position of the heart may have been responsible for the absence of diagnostic signs in Lead aV_F of the localized posteroapical infarct in Case 18. The diagnostic failures in the other three cases were attributable to horizontal position of the heart.

In old, as in recent anteroposterior infarction, diagnostic failures were much less frequent when the lesion involved the apical one-half or more of the posterior wall than when it was limited to the apical one-third. The findings in Lead aV_F were diagnostic of posterior infarction in four of the eight cases with a healed lesion of the apical one-half or more of the wall (Cases 51, 63, 67, and 96), suggestive in three (Cases 64, 66, and 86), and negative in one (Case 152), as a result of the horizontal position of the heart.

Correlation of Electrocardiographic and Pathologic Findings Associated With Independent Anterior and Posterior Infarcts.—Anatomically separate anterior and posterior infarcts were found in eleven cases. In four of these (Cases 59, 91, 94, and 127), there was a recent extensive posterior infarct, accompanied by a healed subendocardial anteroseptal lesion, the anterior lesion occupying the apical two-thirds of the anteroseptal wall in Case 59 and being confined to the apical one-third in the other three cases. The electrocardiogram was diagnostic of the recent posterior infarct in all four cases and of the anterior lesion, as well, in Case 59. The precordial leads revealed abnormalities in the initial deflection which were strongly suggestive, but not pathognomonic, of old anteroseptal infarction in Cases 91 and 94. The QRS-T pattern in the precordial leads in

Case 127 was typical of extension of the posterior infarct and associated pericarditis into the lateral wall of the left ventricle, but failed to reveal the old anteroseptal lesion.

In four cases (Cases 60, 73, 129, and 151), there was a recent anterior infarct, diagnosable from the precordial leads. This anterior infarct was accompanied by an old posterior infarct, recognizable from Lead aV_F in Cases 60 and 129, but not in the other two cases, because of the horizontal position of the heart. Although the potential variations of the left leg in Case 60 also were transmitted principally from the right side of the septum and right ventricle, as a result of the horizontal position of the heart, the extension of the posterior infarct into the septum was recognizable from the abnormal Q wave preceding the small R and deep S waves of Lead aV_F.

Separate healed anterior and posterior infarcts were found in the other three patients (Cases 45, 68, 82). The precordial leads revealed diagnostic signs of the anterior lesion in the two former, but not in Case 82, as a result of left bundle branch block. Lead aV_F revealed suggestive evidence of the posterior lesion in Case 68, but not in the other two cases, because of the horizontal position of the heart.

Electrocardiographic differentiation of simultaneous from consecutive anteroposterior infarction was impossible after healing and was difficult even in the acute stage. The typical pattern of acute anteroposterior infarction, characterized by the concurrent registration in leads from the left leg and precordium of abnormal Q waves together with RS-T elevation (or cove T-wave inversion), may be simulated by (1) recent posterolateral infarction, and (2) acute anterior or posterior infarction accompanied, in the opposite wall, by an aneurysm or an old infarct with recent pericarditis. Differentiation is usually possible when serial tracings are available.

RS-T depression in the precordial leads is a familiar reciprocal manifestation of recent posterior infarction, but was found in only three of the thirty cases of acute posterior infarction accompanied by recent or old anterior infarction. The downward RS-T displacement in two of these cases (Cases 38 and 58) was adequately explained by the demonstration of a recent infarct in the subendocardial portion of the anterior wall and was more likely a secondary manifestation of a conduction defect in the anterior wall in the other case (Case 59). Acute RS-T depression in Lead aV_F is a familiar manifestation of recent anterior infarction, but was not found in any of the twenty-eight cases in which the acute anterior infarct was accompanied by a recent or healed posterior infarct. However, RS-T depression was found in Lead aV_F in one case (Case 47) in association with recent extension of an old anterior infarct into the lateral wall.

Findings in the standard leads were strongly suggestive of combined anteroposterior infarction in only four of the fifty-two cases (Cases 31, 53, 65, and 127). In Case 53, the QS pattern in Leads II and III was probably unrelated to the relatively small posteroapical infarct and was actually due to reference of the potential variations of the right ventricle and/or infarcted anteroapical wall of the left ventricle to the left leg. In Case 127, the pattern in the standard leads was a manifestation of the acute posterolateral infarction. The standard

leads furnished suggestive to diagnostic evidence of the anterolateral, but not the posterior lesion in fifteen cases, and comparable evidence of the posterior, but not the anterior infarct in twenty cases. The standard leads were not indicative of either lesion in the remaining thirteen cases. Thus, the standard leads alone were of very limited value in the diagnosis of combined anteroposterior infarction.

SUMMARY

The findings in the Wilson precordial leads and in the standard and Goldberger limb leads have been analyzed and correlated with the pathologic findings in fifty-two cases of coexistent infarction of the anterior and posterior walls of the left ventricle. Autopsy revealed a recent infarct involving the apical one-third or more of the anterior wall and continuing through the septum and around the tip of the left ventricle into the apical one-third or more of the posterior wall in twenty cases, and an old healed infarct of similar distribution in sixteen cases. The pathologic findings were the result of the confluence of independent anterior and posterior infarcts in at least three of these thirty-six cases, and were attributed to simultaneous anteroposterior infarction in the other thirty-three cases because of the anatomical continuity of the lesions and the uniformity in age. Five additional cases were observed with pathologic evidence of simultaneous anteroposterior infarction, complicated by a separate posterobasal lesion. The eleven remaining cases had anatomically separate anterior and posterior lesions.

The cases were classified according to the extent of the involvement of the posterior wall into two groups: (a) twenty-two cases of infarction confined to the apical one-third and (b) thirty cases of infarction of more than the apical one-third of the posterior wall. Electrocardiograms were obtained during the acute phase of the posterior infarct in fifteen cases of each group.

Lead aV_F proved very disappointing for the detection of extensions of a large anterior infarct into the apical one-third of the posterior wall. The pattern in this lead was considered diagnostic of posterior infarction in only two cases, intermittently diagnostic in another, suggestive in three, and negative in sixteen. The negative findings in twelve cases were ascribed to horizontal position, which favored transmission of the potential variations of the right ventricle to the left leg. The negative findings in the other four cases occurred despite intermediate to semivertical position of the heart and were attributable to one or both of the following factors: (1) derivation of the potential variations of the left leg chiefly from those of the intact basal two-thirds of the posterior wall of the left ventricle, and (2) marked reduction in the opposing negative cavity potentials available for transmission through the infarcted apical one-third of the posterior wall, as a result of the extensive lesion of the anterior wall and septum. The influence of cardiac position in one case of infarction of the apical one-third of the posterior wall was exemplified by the registration of an abnormal QR complex in Lead aV_F when the heart was in intermediate position and its replacement by a notched R wave when the heart shifted into a vertical position.

Lead aV_F was a much greater help in the detection of infarcts involving more than the apical one-third of the posterior wall. The findings in this lead were considered diagnostic of the lesion of the posterior wall in eighteen cases, suggestive in five, and negative in the other seven because of the horizontal position of the heart. The continuation of the apical infarct into the middle one-third of the posterior wall increased the incidence of positive findings in Lead aV_F.

In one case from each group, the findings in Lead aV_F were classed as negative despite fulfillment of the requirements for a diagnosis of posterior infarction. A study of the unipolar limb lead in reference to the precordial leads in these cases indicated that the findings in Lead aV_F were not due to the posterior lesion, but rather were representative of the potential variations of the infarcted septum, transmitted through the right ventricle to the leg as a result of horizontal position.

Typical signs of anteroseptal infarction originally present in one case were obliterated with the development of an extensive posterior infarction. The absence or paucity of diagnostic signs in the precordial leads referable to the anterior infarction in four other cases was regarded as a secondary manifestation of a large posterior infarct and was attributed to reduction in the opposing negative cavity potentials available for transmission through the anterior wall. On the other hand, infarcts limited to the apical one-third of the posterior wall caused no demonstrable alteration in the precordial lead patterns referable to the anterior lesion.

Acute RS-T depression in the precordial leads, which is a familiar reciprocal manifestation of recent infarction limited to the posterior wall, was observed in only three of the thirty cases of acute posterior, coupled with recent or old anterior infarction. The downward RS-T displacement in these cases was regarded as a direct manifestation of subendocardial anterior infarction. Furthermore, acute RS-T depression was not found in Lead aV_F in any of the twenty-eight cases in which acute anterior infarction was accompanied by a recent or old posterior infarction.

The standard limb leads were of very limited value in the diagnosis of coexistent anteroposterior infarction. The findings in these leads were not indicative of either lesion in thirteen of the fifty-two cases, and were strongly suggestive of both in only four cases. However, the pattern compatible with anteroposterior infarction was considered a manifestation of posterolateral infarction in one of the latter, and a result of anterolateral plus septal infarction in another.

The electrocardiograms were taken by Miss Josephine McDonald and were retouched by by Miss Evelyn Erickson and Miss Geraldine Chesney.

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HYPERTENSION AND TACHYCARDIA DUE TO CONCUSSION OF THE BRAIN

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DESPITE the existence of a rather extensive literature on the "postconcussion syndrome," no reference was found in the Anglo-Saxon reviews on this subject concerning neurovegetative manifestations of the types observed in the two cases which will be described. One of them is remarkable because of its stormy course; the other is of interest because of the opportunity afforded for systematic study of central vasomotor irritability tests.

CASE REPORTS

CASE 1.*—A. K., a 31-year-old, unmarried, white woman, was injured in an automobile accident on Sept. 1, 1947, and shortly thereafter was admitted to the Mary Fletcher Hospital, Burlington, Vt., in a semiconscious state. According to her history, which was taken at a later stage, she had always been well except for scarlet fever with possible renal involvement at the age of 9 years. Menstruation was normal. During World War II she served in the United States Armed Forces as a WAAC and repeated routine medical examinations had not revealed any abnormalities. The blood pressure had been found to be "normal."

On admission to the hospital she was in a state of shock and in pain. X-ray examination revealed multiple fractures of the pelvis, fractures of the fourth, fifth, sixth, and seventh ribs and of the transverse processes of the fourth and fifth lumbar vertebrae. There was no fracture of the skull, but a slight prominence of the right squamous suture, suggesting diastasis, and a laceration of the skin above the right eye were present. The right eye deviated laterally. No nystagmus was seen. No abnormalities of the other cranial nerves were observed, but a transient left hemiparesis was noted for about one week.

On September 3 the pressure of the lumbar fluid was 300 mm. H_2O and the fluid appeared slightly bloody. Ten days later the pressure was 210 mm. H_2O, the cell count 144 per c.mm., and the total proteins were 30 milligrams per cent. The red blood cell count was 3,130,000 with 68 per cent hemoglobin. The leucocyte count was 53,200 with polymorphonuclear cells prevailing. It fell within five days to 8,900 with a normal differential picture. Serum proteins were 5.8 per cent. The nonprotein nitrogen was 34 mg. per cent. The urine contained many red cells on admission and at times there were traces of albumin and sugar. The specific gravity varied between 1.007 and 1.025. During the following weeks a considerable number of pus cells and colon bacilli appeared in the urine.

Immediately after admission she was able to answer some questions but had no recollection of the accident and was not sure of her own name. During the first eleven days she was irrational most of the time and very talkative, with emotional outbursts and considerable crying and screaming. During the following week she became more rational during the daytime but was noisy

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Received for publication Jan. 23, 1948.

*The author is indebted to the attending physicians of this patient, Dr. K. F. Truax, Dr. R. M. P. Donaghy, and Dr. L. Wallman for permission to study and publish this case.

and even aggressive at night. These mental abnormalities disappeared gradually, except for a certain moodiness and talkativeness.

The basal metabolic rate was +15 on September 20, +20 on October 20, and −11 per cent on November 12. The electrocardiogram taken on September 15 showed normal standard leads with a high T wave in Leads I and II. In Leads CF_1 and CF_2 the T wave was inverted. On October 10 the T wave was inverted also in Lead CF_3 and low and diphasic in Lead CF_4.

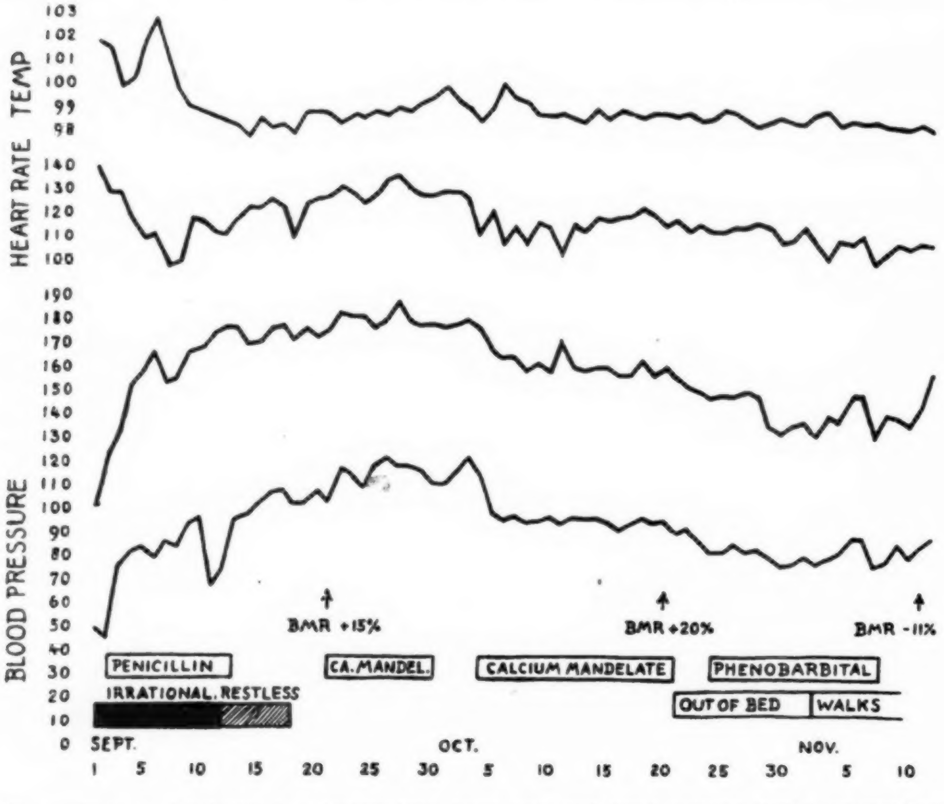

Fig. 1.—Case 1. Fluctuations of temperature, heart rate, and blood pressure during seventy-four days following concussion of the brain.

Determination of epinephrine and related compounds (sympathin, encephalin) in the blood and spinal fluid* showed concentrations near the upper limit of normal (225 and 198 color units per cubic centimeter, respectively) on October 22. On November 11 the blood level was still almost as high (215 color units per cubic centimeter).

The fluctuations of the temperature, heart rate, and blood pressure are indicated in Fig. 1 in which each point represents the daily average of measurements taken almost every hour. The initial leucocytosis, fever, and low blood pressure were obviously due to hemorrhage and shock. Later slight elevations of the temperature coincided with a mild urinary infection which was controlled by calcium mandelate medication.

For about seven weeks the systolic and diastolic pressures remained at a hypertensive level with only minor acute oscillations; however, a gradual return toward normal set in after four weeks and was about complete nine weeks after the accident. Repeated intramuscular and intra-

*Colorimetric method of F. H. Shaw (Biochem. J. 32:19, 1938), slightly modified by W. Raab (Exper. Med. & Surg. 1:188, 1943; Biochem J. 37:470, 1943).

venous injections of 0.5 to 1.0 mg. of dihydroergotamine (DHE 45) did not affect the high blood pressure level, while intravenous injection of Pentothal (8.0 c.c. of a 2.5 per cent solution) caused an immediate fall of the blood pressure from 169/87 to 114/60. Functional tests for central vasomoter irritability which had been exaggerated at first gave normal responses when the blood pressure had fallen (Fig. 2).

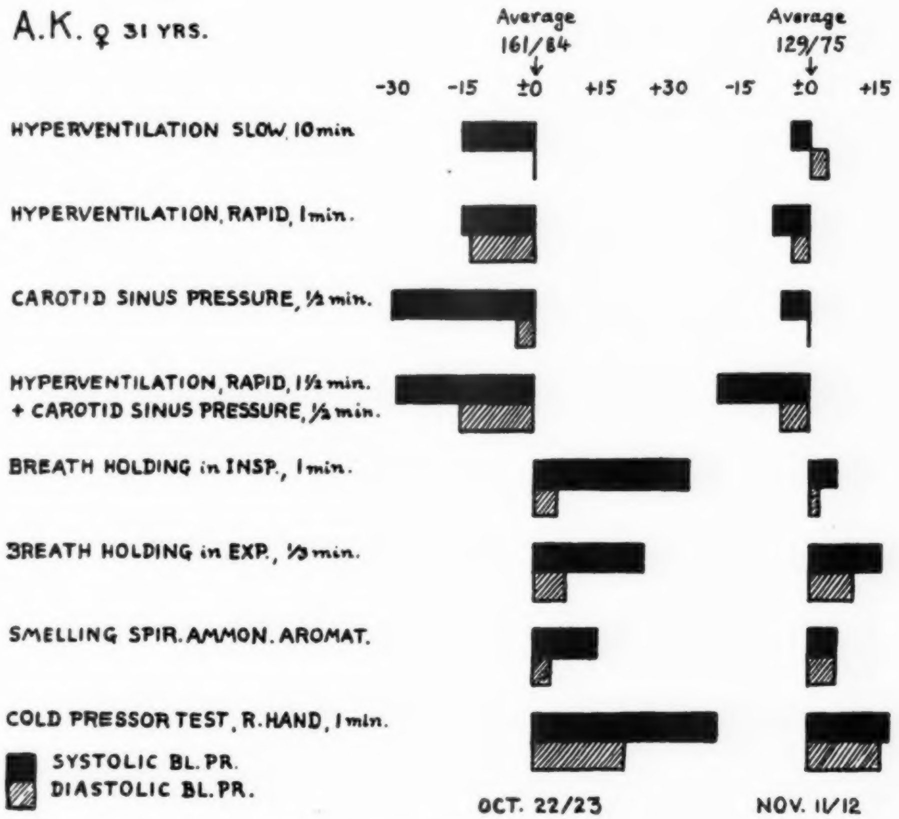

Fig. 2.—Case 1. Response to various tests for central vasomotor irritability during the hypertensive period and after return of the blood pressure toward normal. Falls of blood pressure are indicated by black (systolic) and shaded (diastolic) areas to the left of the zero line, elevations to the right.

The heart rate was rapid (up to 148) throughout her stay at the hospital but showed also a certain tendency to decrease during the last weeks there. The response of the heart rate to carotid sinus pressure diminished simultaneously. At the height of the tachycardia, the intravenous injection of dihydroergotamine and Pentothal had only a slight retarding effect on the heart rate (−16 and −13 beats per minute, respectively).

On November 12 the patient was discharged as she felt quite well and was able to walk with canes.

Case 2.*—S. V., a 45-year-old, married, white woman, a former nurse, entered the Krankenhaus der Kaufmannschaft in Vienna, Austria, where the author was Physician-in-Chief at that time, on Oct. 17, 1938, after having fallen on her head from a ladder from a height of about six feet.

*During her stay at the Second Medical Clinic of the University of Vienna in 1939 and 1940, this patient was under the observation of Dozent Dr. F. Nagl. The data collected during this period and the permission for their publication were obtained through the kindness of Dozent Dr. Nagl and of the present head of the Clinic, Prof. Dr. K. Fellinger, for which the author wishes to express his thanks.

The family history was noncontributory. Menstruation had been regular. She had two children. During World War I she contracted malaria. In 1928 she had a purulent appendicitis, in 1937 a septic sore throat with polyarthritis, pyelitis, and peritonitis, and in 1938 thrombophlebitis and pulmonary infarction. She smoked heavily and consumed liquor to a moderate extent. Before the accident there had been neither signs nor symptoms of the type to be described.

After her accident, the day before admission, she remained unconscious for five and one-half hours and vomited several times upon awakening. On admission she complained of severe headache, nausea, and blurred vision. She appeared apprehensive and slightly disoriented.

On physical examination she was seen to be a well-nourished woman of medium build. The color of the skin and mucous membranes was normal. The head was diffusely sensitive to percussion. The pupils were of normal width and showed somewhat sluggish reaction to light. There was a coarse nystagmus when the eyes were turned laterally. The cranial nerves appeared normal, but the neck was slightly rigid. Peripheral reflexes were normal. The chest and abdomen did not show any abnormalities.

The urinalysis was negative. The red blood cell count was 4,100,000, with a color index of 1.0; the leucocyte count was 5,500 with a normal differential picture. The sedimentation rate was normal. The blood sugar was 88 mg. per cent, the blood cholesterol was 248 mg. per cent, and the blood calcium was 9.6 mg. per cent. The electrocardiogram was normal. An x-ray film of the skull showed normal details. The eye grounds were normal. The Wassermann reaction in serum and cerebrospinal fluid was negative. The cell count and protein contents of the cerebrospinal fluid were normal.

During the first six days in the hospital the patient remained apathetic and complained of intense headaches. The temperature varied between 97.6 and 105.4°F., the pulse rate between 120 and 160 beats per minute (Fig. 3). The blood pressure was 115/70 at first but, together with subsequent paroxysmal rises of the temperature and heart rate, it rose to levels as high as 200/120 (Fig. 3).

During the four weeks which the patient spent in the hospital, such paroxysms of fever, tachycardia, and hypertension occurred nine times, alternating with periods of normal temperature, pulse rate, and blood pressure. The paroxysms began quite suddenly without any obvious cause or stimulus and lasted for several hours. They were accompanied by chills, flushing of the face, and intense perspiration. The patient appeared to be prostrated but, once a paroxysm was over, recovered quickly.

Bacteriological cultures of the blood, withdrawn during fever, remained sterile and no malarial parasites were found. The leucocyte count and sedimentation rate remained unchanged. Amidopyrine (up to 1.0 Gm. per day) did not seem to influence the fever.

Definite abnormalities in the patient's psychic behavior appeared about one week after the accident. She became talkative and alternatingly hilarious and quarrelsome. Finally she left the hospital against medical advice. In a letter written three months later, which she sent to the author who was then in the United States, she mentioned only one more attack on Jan. 22, 1939, when her temperature rose to 104°F., the pulse rate to 180, and the systolic blood pressure to 220 millimeters, and nausea, double vision, perspiration, and temporary unconsciousness were present. Otherwise she claimed to have become well again but complained of having become forgetful, of not being able to recognize people whom she used to know, and of having difficulty in writing. The letter was written in a peculiarly incoherent style and with extremely poor spelling. The same words appeared differently spelled in different places. The letter ended with the words "Heil Hinter!" (instead of "Heil Hitler!", the form of greeting which was compulsory at that time in German-occupied Austria). The fact that her distorted spelling changed the name of the Fuehrer into "Hinter" (behind), indicates her lack of judgment, as it could have been easily misconstrued by the censors as a joke and could have brought her into a concentration camp.

In October, 1939, she had a sore throat, followed by dizzy spells. During one of these spells she fell down a cellar stair on Nov. 17, 1939. This accident resulted in another concussion of the brain and four days of unconsciousness. On November 23, when admitted to the Second Medical Clinic of the University of Vienna, she complained of pain in the chest, left shoulder, and arm.

The objective findings were essentially the same as those which were present in the first accident. She appeared to be in a hypomanic mental state. The head was again tender to percussion, but there was no nystagmus this time. The sedimentation rate was normal and the blood culture was negative. The eye grounds showed a slight compression of the veins at some of the points of arterial crossing. The nonprotein nitrogen was 28 mg. per cent. The cerebrospinal fluid was normal. The basal metabolic rate was +13 per cent on admission.

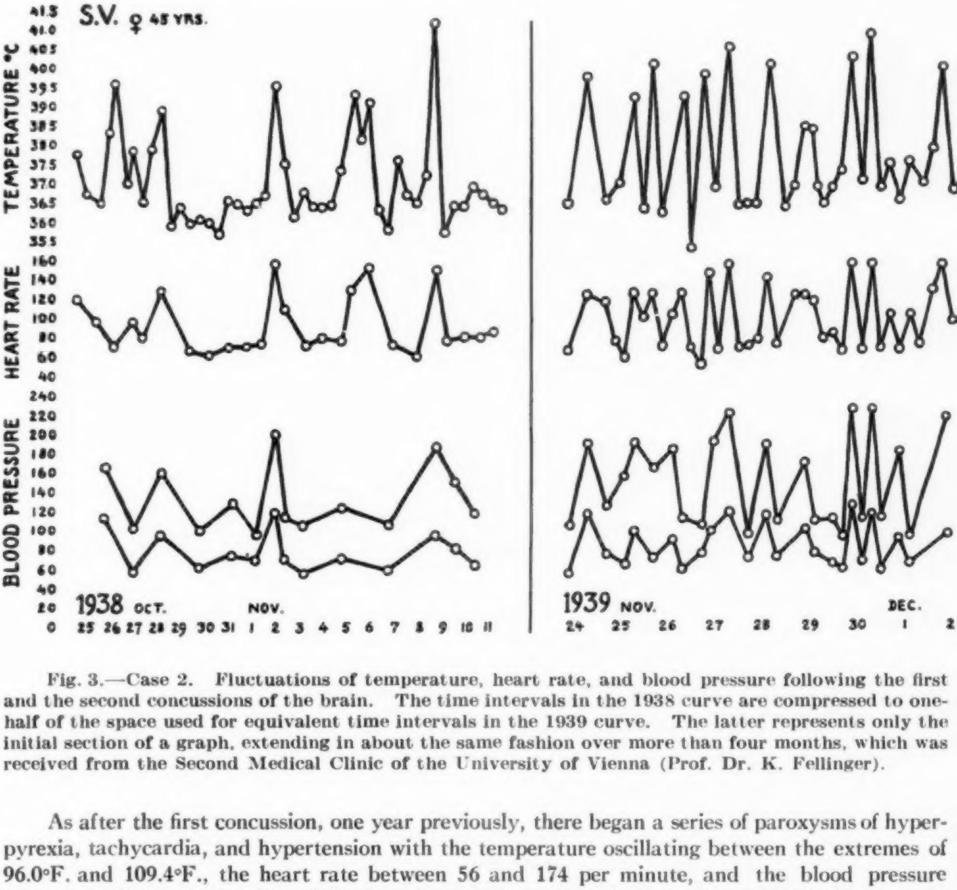

Fig. 3.—Case 2. Fluctuations of temperature, heart rate, and blood pressure following the first and the second concussions of the brain. The time intervals in the 1938 curve are compressed to one-half of the space used for equivalent time intervals in the 1939 curve. The latter represents only the initial section of a graph, extending in about the same fashion over more than four months, which was received from the Second Medical Clinic of the University of Vienna (Prof. Dr. K. Fellinger).

As after the first concussion, one year previously, there began a series of paroxysms of hyperpyrexia, tachycardia, and hypertension with the temperature oscillating between the extremes of 96.0°F. and 109.4°F., the heart rate between 56 and 174 per minute, and the blood pressure between 98/65 and 240/130. Following the second accident, these attacks, of which 101 occurred within 133 days of hospital observation, were accompanied by chills, perspiration, mental disturbances, and prostration. At times the muscles of the back and neck were rigidly contracted and tonic and clonic spasms occurred. Some of the attacks lasted for only thirty minutes; others, for one to two days. Some of them were elicited by emotional excitement.

Injections of Hexeton, Pantopon, Novalgin, Agrypnal, Dolantin (Demerol), Luminal, aminophylline, and insulin produced no distinct effect, nor did x-ray irradiation (five sessions) over the hypothalamic area. Only after the intravenous injection of 4.0 c.c. Evipal was there an immediate fall of blood pressure and pulse rate, but this effect lasted only a short time.

The basal metabolic rate was again determined on Feb. 22, 1940, and followed through an attack (Fig. 4). It was +52 per cent when the temperature was still normal. Subsequently it fell to zero when the fever was at its peak and rose again with falling temperature to a maximum of +92 per cent. On Feb. 27, 1940, the basal metabolic rate was +13 per cent with a temperature of 98.2°F.; it fell as low as −14 per cent when the temperature rose to 102.4°Fahrenheit.

On April 3, 1940, the patient was discharged from the hospital. She had lost 14 pounds of weight during her stay there. According to a letter received from her by the author, dated Nov. 14, 1946, she had been entirely free of symptoms during the years 1941 through 1945 and had been married for the second time. However, during 1946, when living conditions in liberated Vienna grew increasingly desperate and she was exposed to various hardships, some attacks of fever occurred again. The letter written in 1946 does not show the errors in spelling displayed in the one of 1939.

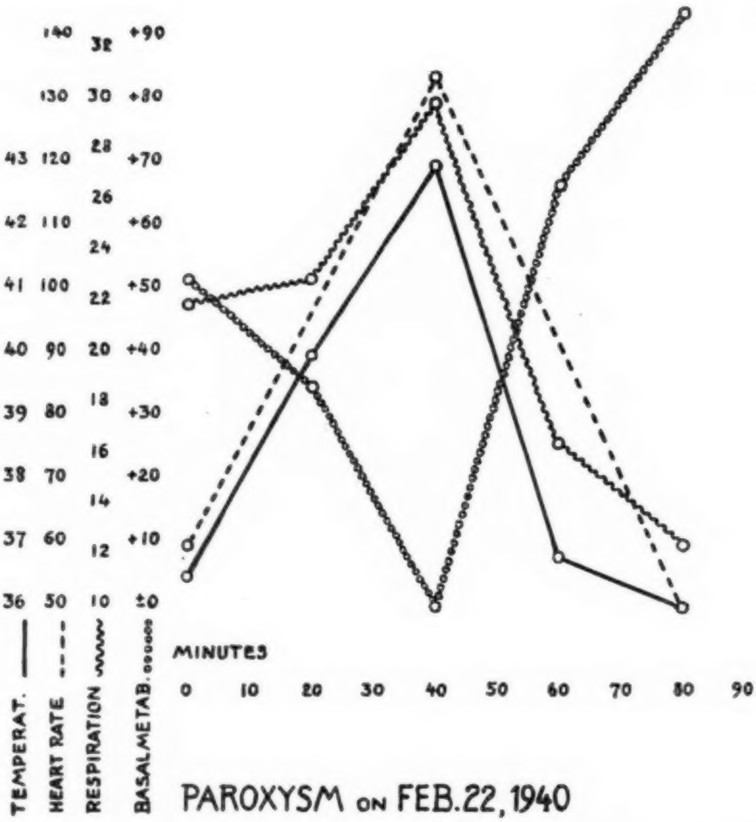

Fig. 4.—Case 2. Changes of temperature, heart rate, respiration, and oxygen consumption during a paroxysm. (This graph is based on data received through the courtesy of Prof. Dr. K. Fellinger, head of the Second Medical Clinic of the University of Vienna.)

DISCUSSION

The neurovegetative manifestations, observed in the two cases of cerebral concussion which have been presented, differ in certain respects. The first patient developed a sustained hypertension which persisted for several weeks and declined gradually. It was accompanied by a permanent tachycardia but no significant elevation of temperature which would have been attributable to the cerebral injury as such. In the second patient there were numerous paroxysms of hypertension, tachycardia, and hyperpyrexia, alternating with fairly normal

conditions, except for some mental disturbances, and subsiding spontaneously, only to be provoked anew and for a much longer period by a second concussion.

Hypertension.—Temporary elevations of the blood pressure following direct cerebral injury are not uncommon[2,3,4,5] but have been described in only a very few cases of mere cerebral concussion. In one case, a 35-year-old man developed a systolic hypertension of 250 mm. after having fallen and struck his head.[6] In another case, a 43-year-old man fell on the occiput and three months thereafter had a blood pressure of 235/140 which slowly declined during bed rest and medication with Luminal.[7] Marburg[8] mentions an occasional rise of the blood pressure of young people after concussion (to systolic levels of 140 to 150 mm.), but such reactions are said to be infrequent.[9] In one instance of electric shock a rise of the blood pressure to 230/155, occurring eleven weeks later, was attributed to a lesion of the vasomotor centers.[10] Prolonged periods of hypertension, some of them terminating in death, have been observed in cases of poliomyelitis which affected the upper medulla oblongata, especially the substantia reticularis grisea,[11,12] and after encephalitis.[37] Paroxysms of arterial hypertension have been described by Penfield[13] in his classical case of "diencephalic autonomic epilepsy" due to a tumor near the foramen of Monroe which pressed on both thalami, by Engel and Aring[14] in a case of a small cystic lesion of the hypothalamus, and by Weber[15] in a case of subacute meningococcic meningitis. Hypertension in connection with increased intracranial pressure[1,51] and after encephalographic air insufflation into the brain ventricles[9,52] has been observed repeatedly. The syndrome of "blast hypertension," recently described by Ruskin and his associates,[50] appears to have been caused by emotional psychosomatic factors rather than by actual physical injury to the brain.

All of these observations are strongly suggestive of the possibility that hypertensive states, prolonged or paroxysmal, can originate in the vasoconstrictor centers of the brain and medulla. In our first case the outcome of a number of tests which specifically indicate an abnormal degree of central vasomotor irritability, such as hyperventilation,[16] carotid sinus pressure,[17] a combination of both,[18] breath-holding,[19] the smelling of ammonia,[18] and the cold pressor test,[20] was in keeping with the assumed central nervous origin of the hypertension when the arterial blood pressure level was high (Fig. 2). After the arterial blood pressure had returned toward normal, the sensitivity tests also evoked responses within or near the normal range. In Beiglböck's[6] case of hypertension after concussion, the hyperventilation test was applied by the present author and was found to indicate a state of abnormal central vasomotor irritability. Whether or not the potent sympathomimetic vasoconstrictor amine "encephalin" which has recently been isolated from the brain, especially from the basal ganglia,[21] participates directly in centrogenic vasoconstriction remains to be investigated.

The hypertensive paroxysms of the second patient resembled those observed by Penfield[13] and by Engel and Aring[14] in their cases of autonomic diencephalic epilepsy. On the other hand, although no direct positive evidence in favor of a pheochromocytoma was obtained, the possible presence of such a tumor in

the second patient and a post-traumatic "centrogenic" stimulation of its secretory activity must be kept in mind. In a case described by Washington and his co-workers,[23] hypertension with attacks of vomiting and headache developed suddenly four months after the patient had fallen on his head and had been treated for one week in a hospital. A pheochromocytoma was suspected and verified by operation, during which the patient died. The authors do not claim any causal connection between the head injury and the onset of the hypertension, however. Even more problematic is the existence of such a causal connection in a case described by Mortell and Whittle.[24] Certain observations by Freeman and Jeffers,[25] by Elaut,[26] and by Drake and associates[36] suggest a stimulating effect of cerebral anoxia and cerebral injury upon the secretory activity of the adrenals. Dolgin[27] ascribes the sudden death of a young soldier, five days after a slight, seemingly harmless head injury, to the presence and activation of a previously asymptomatic pheochromocytoma which was found at autopsy.

Tachycardia.—Tachycardia, persistent as in Case 1, or paroxysmal as in Case 2, has been described as a sequel of encephalitis,[28,29,37] in autonomic epilepsy due to tumors and cystic lesions in the thalamic area,[13,14,30] and in one case of concussion in which cavity formation and gliosis were found in the brain stem.[31]

Although there was a strict coincidence of the paroxysms of tachycardia with those of hypertension in Case 2, these phenomena do not necessarily appear together always. In Case 1, for instance, the trend toward normalization of the heart rate did not keep pace with that of the blood pressure level; the response of the tachycardia to intravenous Pentothal was insignificant compared with that of the blood pressure. In contrast, dihydroergotamine depressed the heart rate more than the blood pressure. Marburg[8] regards a discrepancy between heart rate and blood pressure level as an "important sign of recovery from a concussion."

The electrocardiographic changes seen in Case 1 may possibly be interpreted as indicating myocardial damage of the type usually caused by an exaggerated action of the anoxia-producing sympathomimetic amines, epinephrine and sympathin.

Hyperpyrexia.—The two elevations of temperature in Case 1 were only mild and attributable to hemorrhagic shock and a urinary infection, respectively. The attacks of high fever in Case 2, on the contrary, were clearly connected with the cardiovascular paroxsyms and reached such enormous heights as 43°C. (109.4°Fahrenheit). They were usually preceded by severe chills and accompanied by profuse perspiration and prostration. In this respect they resembled the paroxysms of fever in the concussion case of Cox,[31] in a case of permanent hypertension after encephalitis,[28] in the case of hypothalamic attacks of Engel and Aring,[14] and in cases of pheochromocytoma.[22]

Basal Metabolism and Respiration.—In Case 1 there was a moderate increase of the basal metabolic rate which disappeared as the hypertension decreased (Fig. 1). The behavior of the basal metabolic rate in Case 2 was surprising in so far as it was elevated during the afebrile intervals but was recorded as being zero or below zero when the fever rose to its peak; and only with a return of the

temperature to normal did the basal metabolic rate reach a level of +92 per cent (Fig. 4). The readings of zero and of −15 per cent obtained during paroxysms of fever must be regarded with skepticism as they seem incompatible with Van t'Hoff's law, even if the fever at this stage may have been largely due to heat storage through surface vascular constriction rather than to actual heat production alone. The rapid respiration during the paroxysms of fever may have been accompanied by a sucking in of some atmospheric air near the edge of a not quite tightly fitting mouthpiece.

In Harrer's as yet unpublished case of postencephalitic hypertension and epilepsy[37] the patient had a basal metabolic rate of +160 per cent. In a recent study, Raab and Smithwick[22] have surveyed numerous instances of hypermetabolism in cases of essential hypertension and of pheochromocytoma (up to +142 per cent). They express the opinion that the action of sympathomimetic amines, as oxidation catalysts,[32,33,34] may be made responsible for the increased metabolic rates. Besides, a hypothalamic mechanism regulating respiratory metabolism has been demonstrated experimentally by Grünthal, Mulholland, and Strieck.[35] Rapid breathing was observed in Case 2 during the paroxysms as well as in the concussion case of Cox[31] and in cases of poliomyelitis of the medulla oblongata and of postencephalitic hypertension.[12,37]

Mental Disturbances.—Unconsciousness, followed by agitation, crying, screaming, talkativeness, and by a quarrelsome and at times irrational attitude, was present in both of the cases described in this paper. Similar manifestations have also been observed by Penfield[13] and by McLean[30] in their cases of diencephalic tumors with attacks of autonomic epilepsy.

Muscular rigidity and chronic muscular contractions, as noted in Case 2, are recorded in the observations of Cox[31] and McLean.[30]

The variable symptomatology of hypertensive syndromes of primarily cerebral origin shows in various details a striking analogy with the equally variable symptomatology of other more common forms of hypertension, namely, labile and fixed "essential" hypertension and the paroxysmal or sustained hypertension connected with pheochromocytoma. Blood pressure reactions, such as an accentuated vasopressor response to cold, or an accentuated vasodepressor response to barbiturates, hyperventilation, and carotid sinus pressure, are also more or less frequently seen in essential and in pheochromocytoma-induced hypertension. The same is true for the nonthyrotoxic phenomena of tachycardia and hypermetabolism in these cases.

In a detailed review on the neurohormonal mechanisms apparently involved in both the essential and the pheochromocytoma-induced hypertensive syndrome, Raab and Smithwick[22] have discussed numerous physiological, experimental, and clinical observations which suggest that the syndromes mentioned have one factor in common which seems to be responsible for at least part of their neurovegetative manifestations, namely, an exaggerated activity of sympathomimetic neurohormones (epinephrine, sympathin, and possibly encephalin).

These potent biochemical agents reach their respective effector cells (myocardium and arterial muscular cells) either through the blood stream (epinephrine

and encephalin?) or through direct neurosecretory discharge from the sympathetic terminals (sympathin).[38] Adrenal and sympathetic neurohormonal discharges are controlled largely by diencephalic centers, and sustained arterial hypertension of cerebral origin can be experimentally produced in various ways.[39,40,41,42,43]

The sympathomimetic amines which have just been named are known to exert not only vasopressor and cardioaccelerator effects but also to act as oxidation catalysts and calorigenic agents,[32,33,34,44,45] which makes it probable that they contribute to the hypermetabolic features often observed in the hypertensive syndromes.[22]

Indications of an excess formation of sympathomimetic amines have been found in cases of pheochromocytoma[22] and in essential hypertension[46,47] and may be hypothetically postulated in primarily "centrogenic" forms of hypertension.

The "amphotropic"[48] action of acetylcholine, which simultaneously elicits vagal effects and stimulates adrenosympathetic activity[49] in a delicate and as yet poorly understood equilibrium, may account for certain irregularities and apparent inconsistencies in the manifestations of the neurogenic hypertensive syndromes.

SUMMARY

Arterial hypertension, tachycardia, hyperthermia, tachypnea, hypermetabolism, and mental anomalies, occurring as aftereffects following concussion of the brain, indicate injury to the upper medulla oblongata and the thalamic area. These symptoms may be persistent or paroxysmal and may occur either simultaneously or be dissociated. Two such cases are reported in detail.

The symptoms and signs resemble those which have been described in some cases of brain tumors located near the third ventricle (diencephalic autonomic epilepsy), in cases of encephalitis and of poliomyelitis of the upper medulla oblongata, and in cases of essential hypertension and hypertension induced by pheochromocytoma.

A comparison of the symptomatology of these hypertensive syndromes with the ones due to cerebral injury suggests that all of these syndromes have certain neurovegetative features in common which may be attributed to an excess activity of sympathomimetic amines (epinephrine, sympathin, and encephalin).

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MODIFICATION OF THE ELECTROCARDIOGRAM OF MYOCARDIAL INFARCTION BY ANOMALOUS ATRIOVENTRICULAR EXCITATION (WOLFF-PARKINSON-WHITE SYNDROME)

Report of a Case

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THE difficulty in occasional instances of differentiating myocardial infarction from anomalous atrioventricular excitation (Wolff-Parkinson-White syndrome) has been noted by Levine and Beeson,[1] Palatucci and Knighton,[2] Eichert,[3] and Missal, Wood, and Leo.[4] The paroxysmal tachycardia which occurs so regularly with anomalous excitation may produce chest discomfort which may be mistaken for the pain of infarction, and the electrocardiogram of anomalous excitation may also cause confusion.

Fischer,[5] Zoll and Sachs,[23] Goldbloom and Dumanis,[6] and Rinzler and Travell[24] have reported cases of the coexistence of the two conditions. In these cases electrocardiograms were not recorded during periods when the anomalous excitation reverted to normal excitation, so that there is no comparison between the two, and the effect of anomalous excitation on the electrocardiogram of myocardial infarction cannot be determined.

In the case which is the basis of the present discussion there is definite evidence of the coexistence of the two conditions, and electrocardiograms were recorded shortly after infarction showing both normal and anomalous excitation. These electrocardiograms reveal the fact that anomalous atrioventricular excitation may obscure some of the diagnostic electrocardiographic signs of infarction, in this case, the Q wave. During normal excitation the electrocardiograms showed the characteristic Q_2 and Q_3 of posterior wall infarction. At other times, however, during anomalous excitation the Q_2 and Q_3 were absent, and the initial portions of QRS_2 and QRS_3 were small R waves.

REPORT OF CASE

Summary of Clinical Data.—The patient was a Negro man, 53 years of age, who experienced sudden substernal pressure, palpitation, and shortness of breath immediately following coitus. The substernal pressure, described as indigestion, was moderately severe and lasted about five

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Received for publication Feb. 6, 1948.

hours. The palpitation was prominent and persistent. After the chest discomfort subsided the patient felt extremely weak. About thirteen hours after the onset he vomited once. A physician told him his heart was beating very rapidly. The patient did not recall any previous episodes of palpitation, rapid heart beat, or chest pain. He was admitted to the Veterans Administration Hospital, Washington, D. C., Feb. 5, 1945, the first day of illness.

At this time, physical examination revealed faint heart sounds, a systolic murmur of moderate intensity at the apex, and a very large spleen. The blood pressure was 104/96, and on the second day it was 144/80. The maximum recorded body temperature on the first day of illness was as 99.0°F. (mouth) and rose to 100.8° on the second day. During the next five days the temperature ranged between 99.0° and 99.6°, and then did not rise above 98.6°F. during the next two weeks. The white blood counts were: on the first day of illness, 6,300 per cubic millimeter, with 57 per cent polymorphonuclear leucocytes; on the fifth day, 13,500 per cubic millimeter, with 62 per cent polymorphonuclear leucocytes (20 per cent nonsegmented forms and 42 per cent segmented forms); on the sixth day, 10,300 per cubic millimeter, with 74 per cent polymorphonuclear leucocytes (11 per cent nonsegmented forms and 63 per cent segmented forms); on the eighteenth day, 5,700 per cubic millimeter, with 59 per cent polymorphonuclear leucocytes. Roentgenograms of the chest were interpreted as showing moderate cardiac enlargement. Various studies were carried out to attempt to explain the large spleen without leading to a definite diagnosis. The patient recovered and has suffered no recurrences of chest discomfort, shortness of breath, or palpitation.

The patient was readmitted to the hospital in June, 1947, following a sudden episode of unconsciousness lasting about twenty minutes. He was late for work one morning, and the unconsciousness occurred as he was rushing to catch up with his duties as a messenger in a federal agency. At this time the history was elicited that a few similar episodes of unconsciousness had occurred at the age of 20 years. These previous episodes were associated with biting of the tongue, but none of the episodes was associated with convulsions or incontinence. So far as the patient knew, sudden rapid heart rate did not precede the unconsciousness. No further episodes of unconsciousness occurred over a period of observation of six months. There were no abnormal neurological findings, and no adequate explanation for the rare episodes of unconsciousness was established.

Discussion of the Electrocardiograms.—Electrocardiograms recorded at intervals following the acute episode of chest distress in 1945 are illustrated in Fig. 1. On the first day of illness there was paroxysmal tachycardia. On the second day there were inverted T waves in all leads, a deep Q_3, a Q_2, and depressed RS-T segments in Leads I and IVF. The Q wave in Lead III was abnormally wide, measuring about 0.06 second. On the fifth day, the Q_2 and the deep Q_3, the inverted T_2 and T_3, and the depressed RS-T segments persisted, and T_1 became upright.

The electrocardiogram on the nineteenth day was the first in which anomalous atrioventricular excitation was recorded. There was shortening of the P-R interval and widening of the QRS complex as compared with previous electrocardiograms. These changes are best seen in Leads II and III. The P-R interval on the fifth day during normal atrioventricular excitation was 0.16 second, and the QRS interval was 0.12 second. On the nineteenth day during anomalous atrioventricular excitation the P-R interval was from 0.10 to 0.12 second, and the QRS interval was 0.16 second. In both Leads II and III it can be seen that a small R follows the P wave and the diagnostic Q waves are absent. Judging from the P-R interval in the limb leads, the prominent wave following the T wave in Lead IVF is probably a U wave. The P is probably very low or isoelectric; if the prominent wave following the T wave in Lead IVF

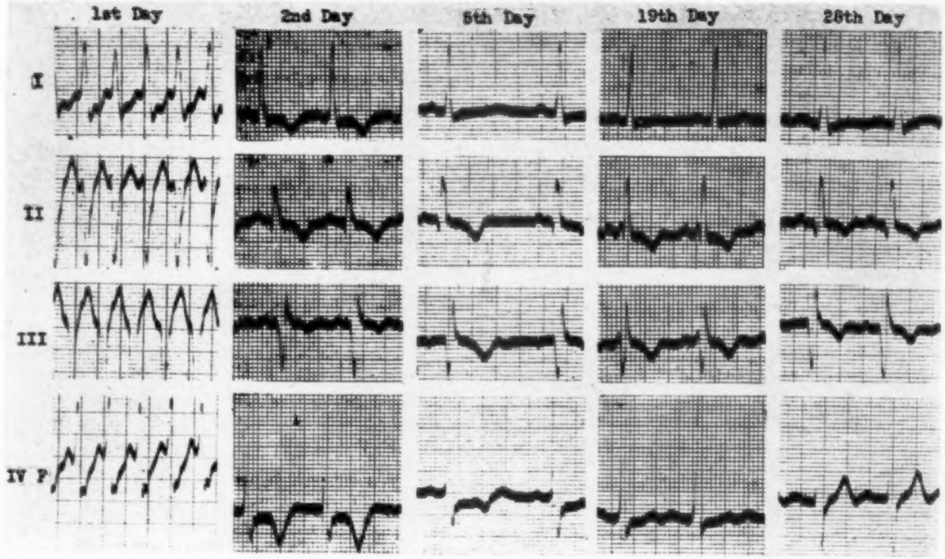

Fig. 1.—Electrocardiograms following the acute episode of chest pain. The number of days following the episode is designated above. The electrocardiogram of the first day shows paroxysmal tachycardia. The electrocardiograms of the second, fifth, and twenty-eighth days are characteristic of recent infarction of the posterior wall of the heart. The electrocardiogram of the nineteenth day shows anomalous atrioventricular excitation (Wolff-Parkinson-White syndrome), and the initial portions of QRS_2 and QRS_3 at this time are small R waves rather than Q waves.

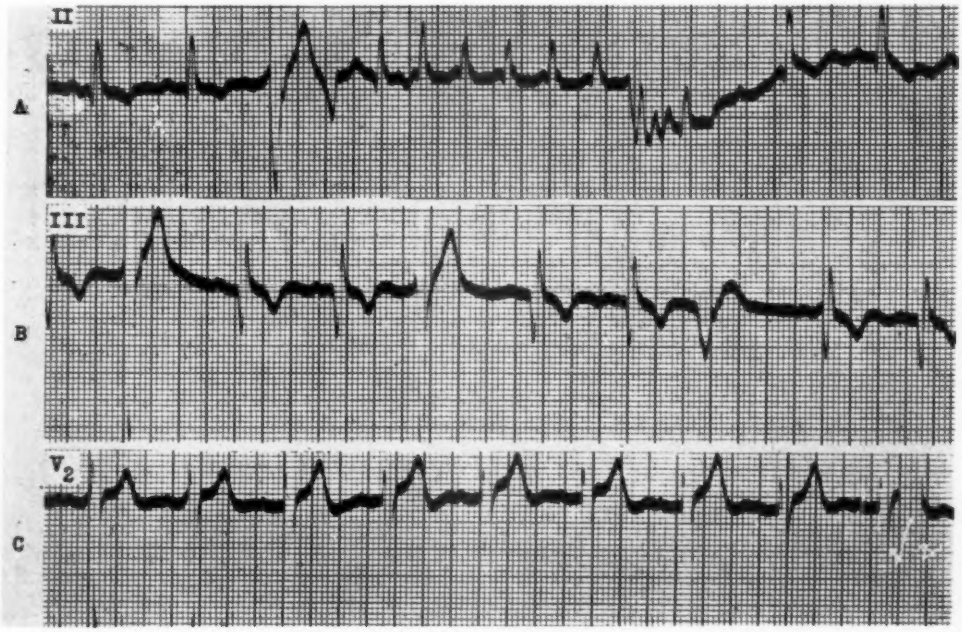

Fig. 2.—Paroxysmal tachycardia initiated by a premature ventricular beat and rapid transitions between normal and anomalous atrioventricular excitation, characteristic of Wolff-Parkinson-White syndrome. *A*, A short run of paroxysmal tachycardia following a premature ventricular beat in Lead II. There is an artefact at the end of the run of tachycardia. *B*, Lead III. Anomalous excitation is recorded in one complex, the next to the last. There are several premature ventricular beats. *C*, Lead V_2. Anomalous excitation is recorded in the first two complexes.

is interpreted as P, that makes the P-R interval disproportionately long even if it is assumed that between the recordings of Leads III and IVF the excitation had reverted to normal. A similar prominent U wave may be seen in Lead IVF of the electrocardiogram taken on the twenty-eighth day following infarction. A slight slur of the first ascending portion of R is observed in Lead IVF in the tracing of the nineteenth day; this became more pronounced in subsequent records of anomalous excitation (Fig. 4).

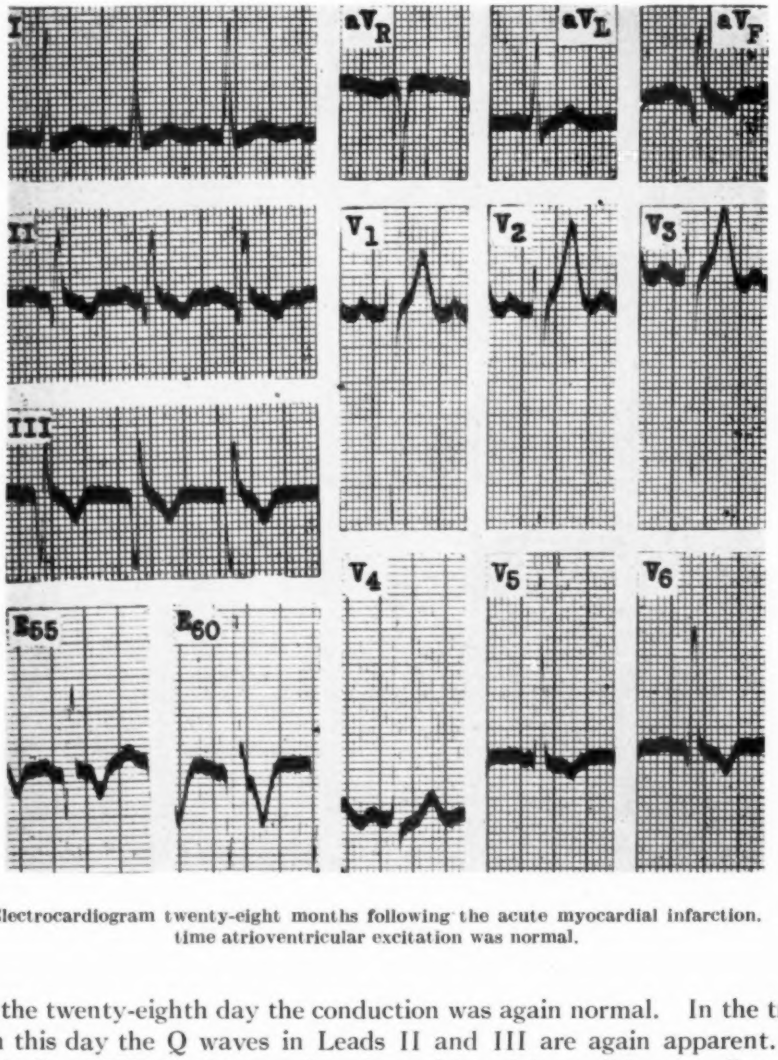

Fig. 3.—Electrocardiogram twenty-eight months following the acute myocardial infarction. At this time atrioventricular excitation was normal.

On the twenty-eighth day the conduction was again normal. In the tracing made on this day the Q waves in Leads II and III are again apparent. The T wave in Lead IVF has become largely upright with possibly a small terminal negative phase. These electrocardiograms were interpreted as being characteristic of infarction of the posterior wall of the heart. The inverted T waves in Leads I and IVF which occurred early and soon disappeared were interpreted as

indicating involvement of the lateral wall or as representing the transient inverted T waves which may occur following paroxysmal tachycardia.[7]

Other electrocardiograms have been recorded following recovery during both normal and anomalous excitation, and these continue to show the differences illustrated in Fig. 1. Q_2 and Q_3 are present when conduction is normal, whereas the initial portions of QRS_2 and QRS_3 are small R waves when anomalous excitation occurs (Fig. 4).

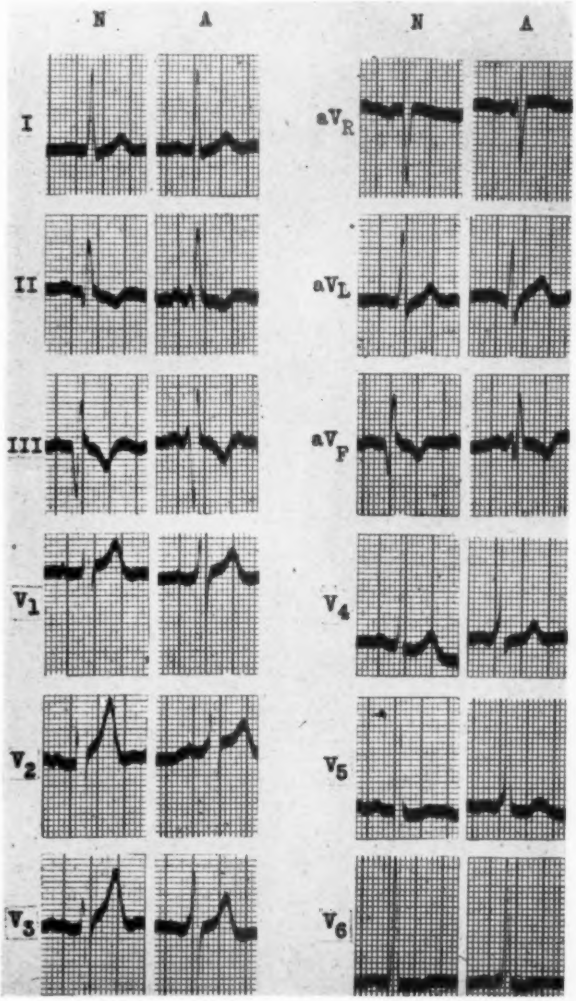

Fig. 4.—Composite of electrocardiograms recorded at various times for comparison of normal (*N*) with anomalous (*A*) atrioventricular excitation.

Fig. 2 illustrates a short paroxysm of tachycardia initiated by a premature beat and rapid changes from normal to anomalous excitation, and vice versa, which are characteristic of the Wolff-Parkinson-White syndrome. In *A*, a short

run of tachycardia initiated by a premature ventricular beat is shown in a strip of Lead II. In *B*, a strip of Lead III, anomalous excitation is recorded in a single complex, the next to the last one. Also, there are several premature ventricular beats. In *C*, a strip of Lead V_2, the first two complexes show anomalous excitation with shortened P-R interval, slurred initial portion of R, and widened QRS complex, while the remainder of the complexes show normal atrioventricular conduction. The T waves of the first two beats are lower than those resulting from normal atrioventricular excitation.

An electrocardiogram made in June, 1947, twenty-eight months after the infarction, at a time when atrioventricular conduction was normal, is illustrated in Fig. 3. The augmented unipolar extremity leads (aV_L, aV_R, and aV_F) were recorded by the method of Goldberger,[8] and the precordial leads (V_1 through V_6) were recorded with Goldberger's modification of the Wilson indifferent electrode.[8] The Q_2 and Q_3 and inverted T_2 and T_3 are still seen to be present, and T is inverted in Leads V_5 and V_6. There is a deep Q wave in Lead aV_F which is consistent with posterior wall infarction.[9,10,11] The tracings marked E_{55} and E_{60} are electrocardiograms obtained with an exploring electrode on a soft rubber tube passed down the esophagus to distances of 55 and 60 cm., respectively, from the nostril, the electrode being paired with the Goldberger indifferent electrode. These leads show the deep Q and inverted T which have been observed in posterior wall infarction.[12]

A composite of electrocardiograms made at different times to compare normal excitation (*N*) with anomalous excitation (*A*) in the various leads is illustrated in Fig. 4. The shortened P-R interval and widened QRS complex during anomalous excitation are best seen in Leads II, III, aV_F, and V_2 through V_5. The appearance of a small R as the initial portion of QRS during anomalous excitation is shown in the left leg lead (aV_F) as well as in Leads II and III. The slurring of the initial ascending portion of R during anomalous excitation is quite clear in Leads V_2 through V_5.

DISCUSSION

It is evident that if only electrocardiograms of the type seen on the nineteenth day following the infarction (Fig. 1) were available, the electrocardiographic diagnosis would be impossible. The inverted T waves alone would then be of doubtful significance since inverted T waves occur with anomalous atrioventricular excitation in the absence of cardiac disease and merely as the result of aberrant spread of the excitatory process through the ventricles and the consequent aberrant recovery.

In some individuals the anomalous excitation is very persistent, and it is difficult to obtain records during periods of normal excitation. The electrocardiograms of Fig. 1 show the importance of such records where myocardial infarction is suspected. Sometimes the excitation reverts spontaneously from anomalous to normal, and vice versa, and if electrocardiograms are recorded at frequent intervals the change may be detected. It has been reported that quinidine[13,14] and atropine[15] cause the reversion from anomalous to normal

excitation in some cases. Our experience with a number of cases of Wolff-Parkinson-White syndrome indicates that quinidine is effective, but that atropine is not. From 6 to 9 grains (0.4 to 0.6 Gm.) of quinidine every one to two hours for five or six doses are usually necessary, and such doses frequently produce mild symptoms of cinchonism. Such doses are probably not advisable when acute myocardial infarction is present or suspected, except when paroxysmal ventricular tachycardia complicates this lesion. Late in convalescence, however, the diagnostic use of quinidine appears permissible.

Localization of the Accessory Atrioventricular Pathway.—There is evidence that the syndrome of anomalous atrioventricular excitation may be due to conduction over accessory atrioventricular muscular pathways, and the location of these pathways in the heart may vary.[16,17,18,19] It is important to attempt to localize the accessory pathway in this case after the manner of Rosenbaum and his co-workers,[20] because accessory pathways in different locations may be expected to modify the electrocardiogram of infarction in different ways.

In all precordial leads the positive deflection of the slurred initial portion of QRS during anomalous excitation indicates that the direction of spread of excitation in that part of the myocardium activated earliest is from the dorsal toward the ventral aspect. The interval from the beginning of the P wave to the peak of R is about the same during normal excitation as during anomalous atrioventricular excitation. According to the studies of Lewis and Rothschild[21] and of Wilson, Macleod, and Barker,[22] the peak of R represents the arrival of the excitatory process in the myocardium immediately beneath the exploring electrode. Since in this case the time required for activation of the anterior heart wall (interval from beginning of P to peak of R in the precordial leads) is essentially the same during normal and anomalous conduction, there is no evidence of premature excitation of the anterior wall. The accessory atrioventricular bundle must be elsewhere, probably in the posterior wall or in the septum. If a portion of the posterior wall near the base were connected with the accessory pathway and were uninvolved in the infarction, its early activation by conduction over the anomalous pathway could produce the early R waves in Leads II and III which obscure the Q waves present during normal atrioventricular conduction. Attempts were made repeatedly to complete the electrocardiographic localization of the accessory pathway by electrocardiograms obtained with an esophageal electrode,[20] but this was impossible because in these electrocardiograms anomalous atrioventricular excitation was always absent.

SUMMARY AND CONCLUSIONS

1. A case is reported in which myocardial infarction and the syndrome of anomalous atrioventricular excitation (Wolff-Parkinson-White syndrome) existed together.

2. Electrocardiograms were recorded soon after infarction showing both normal and anomalous atrioventricular excitation. Anomalous atrioventricular excitation may obscure diagnostic electrocardiographic signs of infarction;

in this case, the Q_2 and Q_3 of posterior wall infarction. When myocardial infarction is suspected in the presence of anomalous atrioventricular excitation, it is important to record the electrocardiogram during a period of normal excitation. The transition from anomalous to normal excitation may occur spontaneously or it may be induced in some cases with quinidine. When records during normal excitation cannot be obtained, the electrocardiographic diagnosis of infarction may be impossible.

3. The localization of the premature ventricular excitation in this case is discussed. It is to be expected that the modification of the electrocardiogram of myocardial infarction by anomalous atrioventricular excitation will vary with the location of the premature excitation.

ADDENDUM

Since this paper was accepted for publication, the study of Levine and Burge (Am. Heart J. **36**:431, 1948) has appeared. These authors describe a case of myocardial infarction associated with anomalous atrioventricular excitation, in which, as in the case described here, the anomalous excitation obliterated the characteristic Q_2 and Q_3 of posterior wall infarction.

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DEMONSTRATION OF THE CORONARY ARTERIES WITH NYLON

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THE historical evolution of the corrosion technique for the demonstration of the coronary arteries from the time it first assumed importance as a result of Hyrtl's investigations[1] in 1855 has been outlined by Gross[2] and Whitten.[3]

Most of the variations introduced into the procedure throughout its development have centered about the search for the perfect injection mass in relation to the demonstration desired. Thus, superior penetration could be had at the expense of rigidity, and the converse was also true. Many materials have been forced into the coronary arteries over the past ninety years. The most recent, Neoprene Latex,[4] shows remarkably good penetration but requires supporting chamber casts which obscure the cardiac septa. A combination of the corrosion and radiographic techniques has been suggested recently.[5] This procedure provides a double approach to the precise localization of pathologic change but shares the disadvantages inherent in flexible Neoprene. It is evident that in the absence of a universally suitable injection mass, selection must be made on the basis of qualities that will best serve to illustrate the particular anatomical area of interest.

Our aim was to prepare an anatomical model for teaching the normal coronary circulation by inspection and dissection. The needs were, therefore, (a) that the heart size and configuration and the anatomical relationships of the coronary arteries be preserved without the support of chamber casts; (b) that the model permit of dissection and yet be rigid enough to hold together when partially dissected; and (c) that the penetration include all arteries of macroscopic size. To achieve these ends we have used the synthetic resin, Nylon, as the injection mass. The completed model does, in fact, serve well as the dissection specimen. The monograph of Gross on the blood supply to the heart is used as the dissection manual and all arterial vessels of macroscopic size described by him can be identified, including the terminal precapillary anastamotic network beneath the endocardium (Figs. 3, 4, 5, and 6).

The procedure described here was developed on a large series of calf hearts and is proposed only for this use. Preliminary experience has indicated that the coronary arterioles of the adult human heart will not satisfactorily withstand the injection pressures necessary to produce the same effect achieved in the calf.

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Received for publication Jan. 24, 1948.

For the use specified, the technique is simple and rapid and the results are consistently reproducible.

MATERIALS

A. The Injection Apparatus.—The essential apparatus is illustrated in Fig. 1 and explained in the accompanying legend. This equipment is readily assembled from parts that are available in the average laboratory.

B. The Injection Mass.—This consists of a 10 per cent (weight per volume) solution of alcohol soluble Nylon* in 80 per cent ethanol. Solid Nylon dissolves

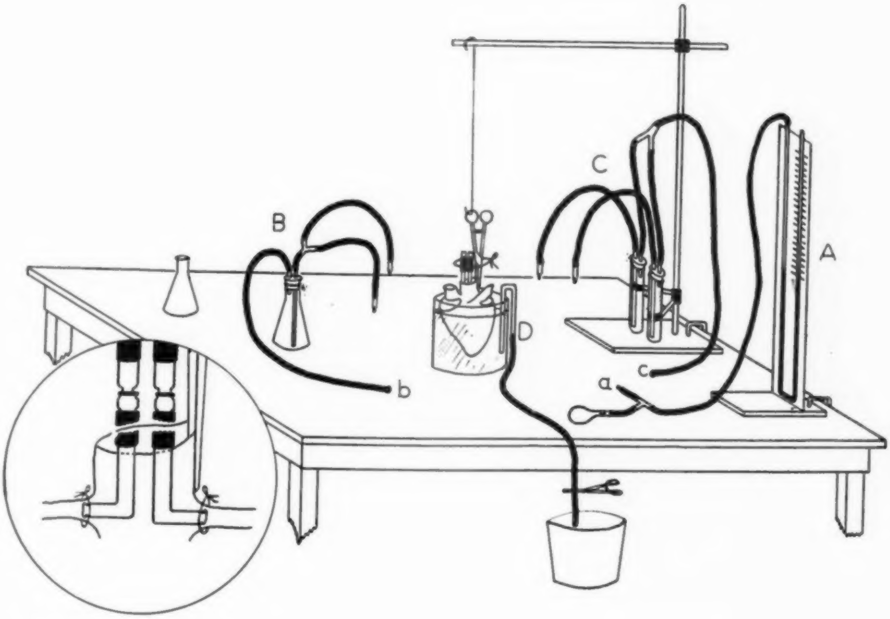

Fig. 1.—Essential equipment.

A, Mercury manometer reading to 500 mm. of mercury. It can be calibrated against a blood pressure apparatus and the scale projected. It serves *B* and *C* in succession.

B, Perfusion Set. The reservoir is a heavy duty 500 c.c. Erlenmeyer flask containing saline. During substitution of the other flask, containing absolute alcohol, the rubber tubing proximal to the Y tube is clamped. The delivery tips are glass tube-to-needle adaptors.

C, Injection Set. The reservoirs are 100 c.c. Pyrex test tubes. The single rubber tube leading to the Y tube is clamped while injection pressure is built up in the manometer, then released to begin the injection. During injection the two-holed stoppers must be held firmly in place by a cork-locking device or by an assistant.

D, Siphon Tube. This is necessary during perfusion for intermittent removal of collected perfusate from the flotation jar.

a is the male member and *b* and *c* are the female members of a metal air-tight joint of the kind used in blood pressure apparatuses.

Because of the pressures employed, all rubber tubing connections must be wired.

Inset. Shows the clamp on the wall of the amputated aorta. The delivery tips are inserted into metal adaptors which connect with the rubber tubing of the cannula assemblies. The right-angled cannulas are made of soft glass. A small flange is provided by the heated tip being impressed on an asbestos pad. The proximal groove is made by the heated tip being rolled on the back of a knife blade.

*Du Pont Nylon FM 6501. E. I. DuPont de Nemours & Co., Plastics Dept., 626 Schuyler Ave., Arlington, N. J.

slowly (48 to 96 hours) at an optimal temperature of 50° to 60° centigrade. Occasional agitation of the container is necessary to break up the mass of partially dissolved resin that forms on the bottom.

The completed solution is water clear with a specific gravity of 0.8814. It is a colloid and when allowed to stand at room temperature progresses slowly from the sol to the gel phase. This change is accompanied by a progressive increase in viscosity (Fig. 2). However, the gel is reversible by immersion of the container in hot water for a few minutes after which the viscosity remains in a workable range for at least six hours. The figure referred to shows the relationship between viscosity and time in terms of absolute units. The relative viscosity is greatly in excess of that of blood, thus necessitating high injection pressures.

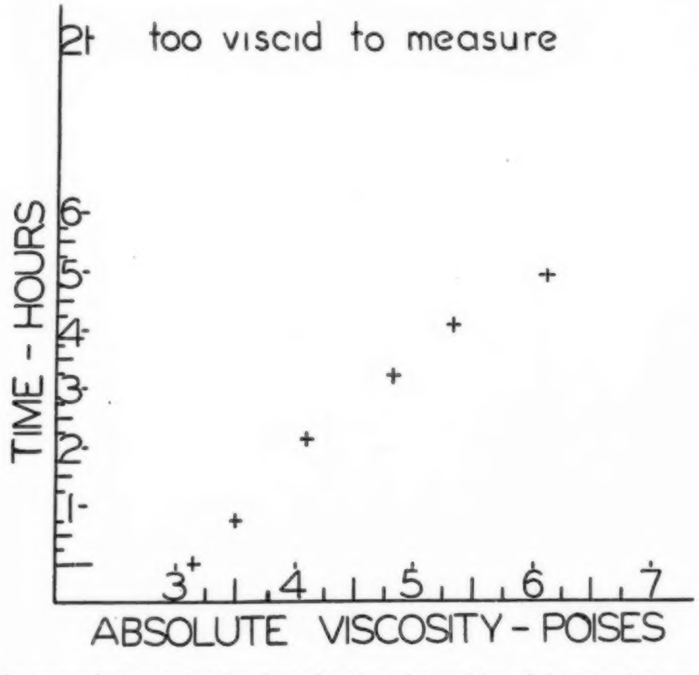

Fig. 2.—The curve demonstrates the time-viscosity relationships of the injection mass, indicating that the rise in viscosity is slow and steady, not affecting significantly the behavior of the injection mass during the first six hours after heat reversal of the gel. Viscosity is given in poises, or absolute units.

Dyes are unsatisfactory for coloring the injection mass. Durable colors are achieved by ball milling pigment pastes into aliquots of the clear Nylon solution.* The desired intensity is obtained by diluting this concentrated stock with additional clear Nylon solution in the ratio of about one to fifteen. It has been the practice in our laboratory to add the colored solution initially, along with the ethanol, to the solid Nylon.

The Nylon solution or gel can be stored in a stoppered container at room temperature.

*Specially prepared to meet the needs of the problem by the Technical Laboratory, Organic Chemicals Department, E. I. DuPont de Nemours & Co., Wilmington, Delaware.

METHOD

A. Preparation of Heart.—The best results were achieved after refrigeration of the heart for forty-eight to seventy-two hours following its removal from the carcass.

B. Cannulation of Arteries.—After exposure of the origins of the coronary arteries by blunt dissection, a double ligature is passed under each orifice, within the outward-sloping aortic wall. The needle is guided around the inferior curve of the coronary orifice under direct vision in order to avoid intimal perforation. One of the two lines thus passed under the orifice is used to tie the cannula in place. A double overhand knot is used to insure a tight ligature that will not slip while the second knot is being tied, thus minimizing the possibility of leakage. So placed, the blunt cannula is in effect applied to the orifice rather than inserted into it and thus will not block the origins of small vessels arising immediately inside the orifice. The second ligature is left free for later use. When both arteries have been cannulated the heart is suspended from an overhead hook by a heavy forceps clamped to the aortic wall over the posterior cusp. The cannulae are then tied to the shaft of the clamp to avoid displacement (Fig. 1).

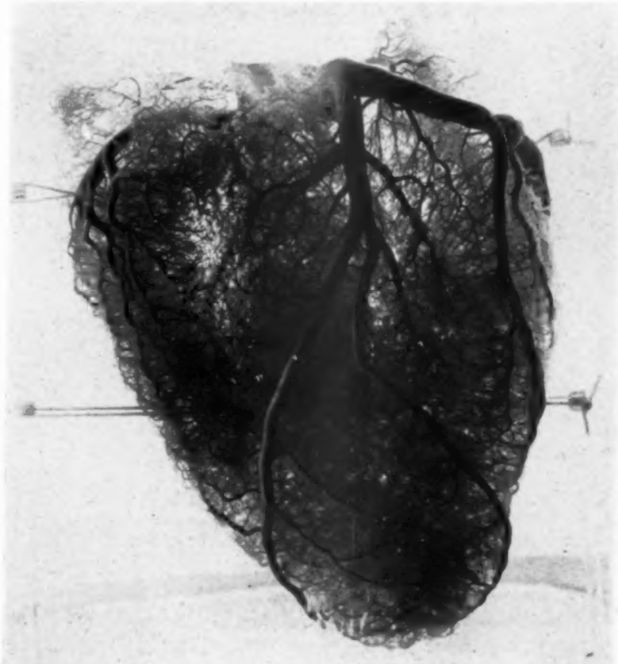

Fig. 3.—The completed specimen. The heart has been rotated counterclockwise and vertically; the largest artery seen is the anterior descending branch of the left coronary artery. This model demonstrates that all coronary arteries of large and medium size are located on the surface of the heart.

C. Flotation and Perfusion of Heart.—The cannulated heart is suspended in tap water at room temperature for support without distortion. The heart is perfused at a pressure of 100 mm. Hg with 500 c.c. of saline and then with an

equal volume of absolute alcohol. We have not found it necessary to perfuse the two arteries separately as suggested by Lieb.[6] Since air bubbles in the arteries can result in discontinuities in the cast, precautions are taken to prevent the admission of air to the system during perfusion and injection. It is convenient to use clamp forceps on the rubber tubing to maintain a closed system when changing perfusion agents. At the completion of perfusion the pressure in the system is returned to zero and gaseous alcohol bubbles are allowed to escape back into the perfusion set before the delivery tips are disengaged. During the alcohol perfusion the small basal vessels severed when the heart was taken from the carcass are identified and tied off.

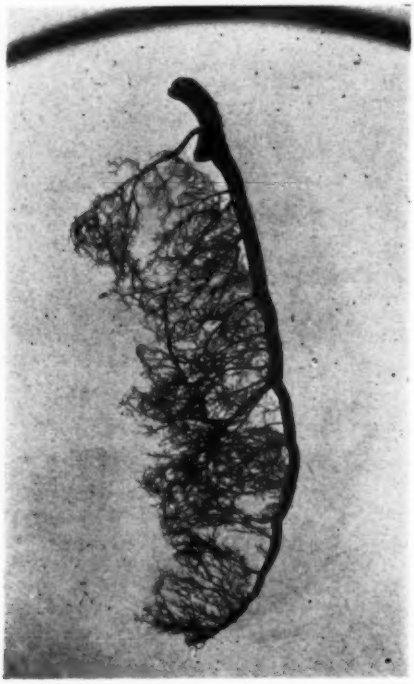

Fig. 4.—An excised artery (first branch of left anterior descending) demonstrating the typical right-angled arrangement and relative caliber of the arteries which penetrate the myocardium from surface sources to subendocardial distribution.

D. Injection.—The delivery tubes of the injection set are filed to their tips, clamped proximally, and connected with the cannulas. After this connection has closed the system, the pressure is returned to zero and the clamps removed. A clamp is then applied to the pressure inflow tube that supplies the Nylon reservoirs and the pressure is raised to 400 mm. of mercury. When this clamp is removed, injection begins. The injection pressure is maintained at the initial height manually by means of the bulb. When the fluid levels in the Nylon reservoirs stop falling rapidly, the pressure is increased to 450 mm. Hg for a few seconds. It is then lowered to 200 mm. Hg and maintained at that height in the

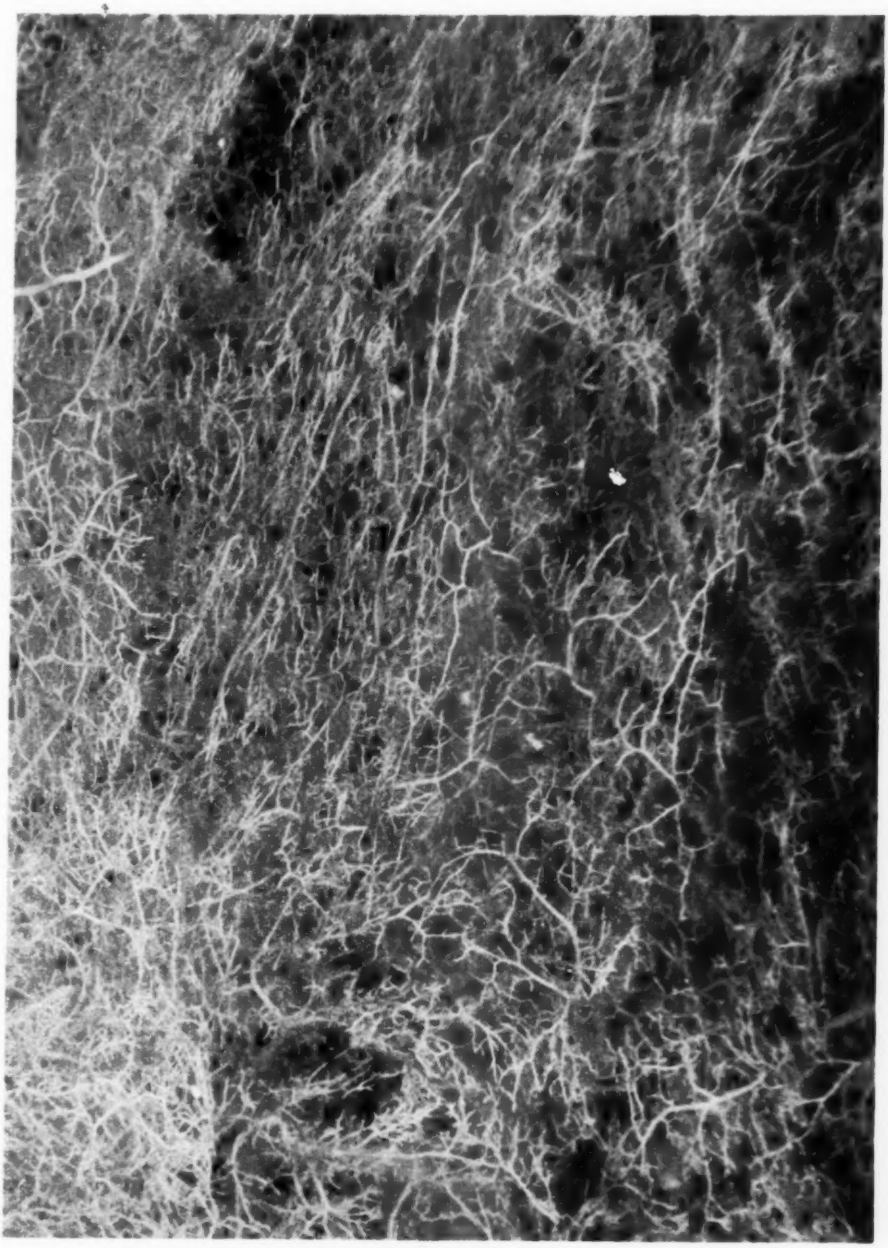

Fig. 5.—Detail of a small portion of the endocardial surface, demonstrating that the penetrating arteries upon reaching a subendocardial level again turn at right angles and pursue a roughly vertical course in that plane, anastamosing freely with one another. Amputation stump of septum at left.

arteries by application of small clamps to the rubber tubing of the cannula assemblies. In the rest of the system it is returned to zero and the delivery tubes are disengaged.

The second ligature originally passed under the coronary orifice is now used to tie off the vessel at the instant an assistant removes the cannula by angulation and traction. This prevents backflow of the injection mass which is still fluid in the proximal end of the artery. When the other artery has been tied off similarly, the heart is inverted to remove collected perfusate and bits of Nylon from the chambers.

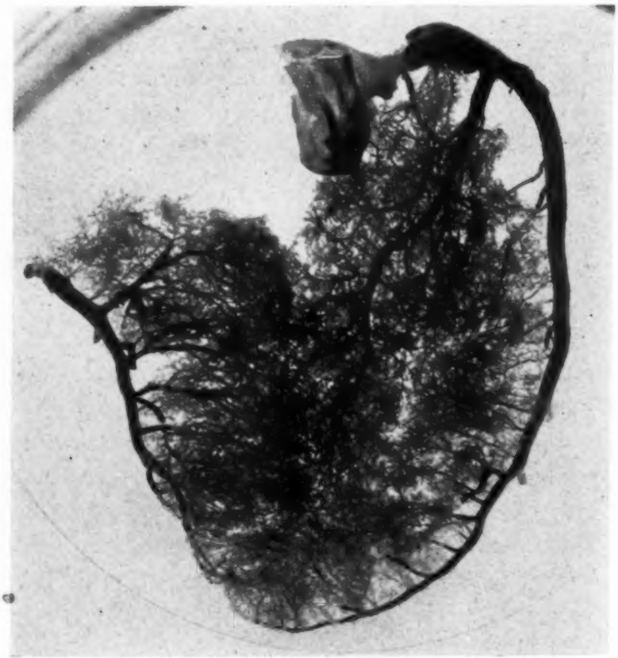

Fig. 6.—Blood supply to the septum. All unrelated vessels have been cut away. The anterior and posterior descending branches of the left coronary artery (Schlesinger[8] Group III arrangement) anastamose with one another just posterior to the cardiac apex. The penetrating branches of each are directed toward the center of the septum. The calf heart is characterized by a separate septal branch which pursues a vertical course through the center of the septum from above. As a rule, it is the first branch of the right artery. In this specimen it originates as the first branch of the left anterior descending artery. Neither arrangement is characteristic of the human heart.

E. Aftertreatment.—The heart is suspended in air overnight by its aortic clamp to complete solidification of the arterial cast. Thereafter, the clamp and all ligatures are removed. The area between the coronary orifices on the intimal surface is covered with a thin layer of clear Nylon solution, a syringe and needle being used that can be inserted into each orifice to bridge the two arterial casts. This bridge furthers orientation by providing a cast of the right and left anterior sinuses of Valsalva and assists in holding the two artery casts together after corrosion.

F. Corrosion.—When the bridge has solidified, the heart is immersed in 20 per cent potassium hydroxide and is not disturbed for five days. At the end of this time the myocardium has dissolved and most of the epicardial fat has formed a syrupy layer of soaps at the surface of the corrosion bath. This layer can be dissolved away readily by a slow stream of water introduced into the bottom of the container and allowed to overflow at the top. After several hours of washing, the cast, now in clear water, is set aside overnight. The next day the washing is repeated to remove additional soaps that have dissolved. Three such washings, alternating with soaks overnight, usually remove all soaps.

G. Mounting.—The completed cast may be stored by being allowed to float freely in a jar of water. It may be manipulated with impunity, but it cannot be lifted above the surface of the water without damage. If the model is to be kept for a week or more it is necessary to add a preservative to prevent the growth of a hazy fungus on the cast. We use a few cubic centimeters of aqueous Merthiolate.

COMMENT

Apart from its value in the preparation of teaching models, this technique shows promise of usefulness in study of the dynamics of coronary flow. For example, when one ties off the left anterior descending branch in its midportion prior to injection, the distal segment and areas normally supplied by the distal segment are found to fill from the *right* coronary artery through anastamoses that are clearly visible in the area of the ventricular wall.

Penetration to the venous side has been seen in only one of a small series of human hearts but not at all in over one hundred calf hearts. In the human heart in which the injection mass penetrated to the venous side, it was of special interest that such penetration occurred in the area of an old myocardial infarction. This isolated observation may support the recent inferences of Prinzmetal and associates[7] regarding the presence of arteriovenous anastamoses in myocardial infarction.

SUMMARY

A technique is described for the preparation of corrosion specimens of the coronary arteries in the calf, employing Nylon as the injection mass. The peculiar advantages of the injection mass and its principal disadvantages are discussed. Several lines of investigation are suggested.

Mr. Clarence E. Peterson assisted in this work from the start and made many practical suggestions which have been included in the final form of the procedure.

Thanks are due to the Technical Service Division of the DuPont Plastics Department at Arlington, N. J., for advice and materials essential to the project.

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THE ELECTROCARDIOGRAM IN VENTRICULAR ANEURYSM

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On a routine electrocardiogram obtained from a patient known to have a ventricular aneurysm, RS-T segments in the precordial Leads CF_2, CF_3, and CF_4 were noted to be elevated (more than 2.0 millimeters). When compared with the patient's previous electrocardiograms, available over a six-year period, these findings were found to be persistent and unaltered. To determine the significance of persistent RS-T segment elevation in the precordial leads, a study of patients with ventricular aneurysm was made. In addition, electrocardiograms were reviewed of those patients in whom ventricular aneurysm was noted at necropsy.

A review of the literature reveals that there is a divergence of opinion concerning specific electrocardiographic patterns in cases of ventricular aneurysm. Sigler and Schneider[1] have stated that the electrocardiogram offered no special help in the diagnosis of cardiac aneurysm, but that "there is a tendency of the major QRS deflection to be directed downward in the second and third lead." Eliaser and Konigsberg[2] believed that there was an electrocardiographic syndrome occurring in 27.3 per cent of twenty-two cases of aneurysm of the left ventricle which could be considered to be a presumptive sign of the lesion. The syndrome consisted of a downward major deflection in Lead I with inversion of the T wave, an upright P wave, and an upright ventricular complex in Lead III. They also described another pattern occurring in 36.4 per cent of their cases and characterized by "downward" directed ventricular complexes in Leads II and III, and a major upright QRS deflection in Lead I. In 18.2 per cent of their cases of cardiac aneurysm the electrocardiogram showed left bundle branch block and there was a large number of equivocal records consistent with disease of the coronary arteries, but otherwise of no significance. Parkinson and associates,[3] in thirteen of their cases of ventricular aneurysm, obtained tracings consistent with infarction of the anterior wall. In only one case was there a Q_3T_3 type of curve indicating posterior wall infarction. According to Nordenfelt,[4] electrocardiographic changes were not so typical of cardiac aneurysms that he could make a direct diagnosis. He suggested that with large aneurysms on the anterior wall of the left ventricle, changes were found which were characterized by a relatively low R_1, deep S_2 and S_3, elevated RS-T segments in all leads, negative T_1, and positive T_2 and T_3. In four of his cases

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Received for publication Jan. 13, 1948.

in which Lead IVF was illustrated, the R wave was absent, the Q-S complex was deep, and the RS-T segment was elevated with a positive T wave. Dressler and Pfeiffer[5] noted that in their cases the usual electrocardiographic stigmata of cardiac infarction were present and that these changes could persist for many years. Fulton[6] believed that electrocardiograms were only of importance in that they added to the evidence of myocardial infarction and assisted in localizing the lesion in the anterior or posterior part of the ventricle. Brams and Gropper[7] felt that electrocardiographic study had revealed various abnormalities but was of no definite aid in the recognition of cardiac aneurysms, and that the electrocardiographic abnormalities could be explained on the basis of the antecedent myocardial infarction. Scherf and Boyd[8] reported that in cardiac aneurysm there is no typical electrocardiogram, but that frequently a rather definite picture was seen which consisted of a very deep Q wave in Lead I and a slightly elevated RS-T segment which appeared to represent a rather recent infarction, except that the pattern persisted for years. Rowland[9] reported that when right axis deviation of the electrocardiogram occurred in a case of otherwise unexplained left ventricular enlargement, the possibility of ventricular aneurysm had to be considered. Gross and Schwedel[10] noted that the single common finding in a group of cardiac aneurysms was the frequent occurrence of right axis deviation thought to be due to right ventricular enlargement resulting from congestive heart failure. It was the impression of these workers that no typical pattern existed for ventricular aneurysm. In none of Crawford's[11] cases were there any patterns typical of cardiac aneurysm, and he believed that electrocardiograms were of help only when they established the existence of a previous coronary occlusion. Master[12] has stated that the combination of intraventricular block, deep Q wave, and inverted T wave in Lead I occurred in about one-third of his proved cases of aneurysm of the anterolateral surface. Fisher[13] in a report reviewing the literature relative to the electrocardiographic changes in ventricular aneurysm, presented a case report of a cardiac aneurysm with rupture in which the electrocardiogram resembled very closely the pattern described by Nordenfelt. Wilson and associates[14] discussed the case of a man who in May, 1941, began to have anginal pain and subsequently developed myocardial infarction. The patient's electrocardiogram exhibited very pronounced RS-T segment displacement, generally associated with recent infarction, and this pattern persisted for about ten months. In this report the investigators stated "that ordinarily pronounced RS-T displacement persists for a few hours or at most a few days." No adequate explanation was offered for the persistence of RS-T segment elevation in the case cited. In the same report a case of Langendorf's was discussed in which persistent RS-T segment elevation was associated with a ventricular aneurysm. In this connection the statement was made that there was "no known reason why ventricular aneurysm should displace the RS-T junction or deform the RS-T segment in this way." Goldberger[15a] described findings which may occur in cardiac aneurysm, but his findings, unlike those to be described by us, apparently can occur in the absence of aneurysm. In a more recent publication[15b] he describes the electrocardiographic findings in fifteen cases of ventricu-

lar aneurysm. All of his patients exhibited an upward QRS complex in aV_R, and he suggests that the absence of this pattern, in the presence of myocardial infarction, excludes aneurysm. Goldberger, however, failed to call attention to significant RS-T segment elevation in the precordial leads of his illustrated cases.

REPORT OF CASES

CASE 1.*—A. D., a 59-year-old white man, was well until January, 1941, when he was admitted to another hospital for severe substernal pain radiating to the left arm. A diagnosis of myocardial infarction was made and confirmed by the typical Q_1T_1 pattern of the electrocardiogram. Recovery was uneventful and he was discharged. He was readmitted on Sept. 15, 1941, because of increasing dyspnea on exertion. The heart was enlarged to the left by percussion with a visible and palpable apex impulse well inside the outer border of dullness. Roentgenkymographic examination confirmed the presence of a ventricular aneurysm.

At this hospital fluoroscopy, kymography, and x-ray study (Fig. 1) were repeated and the presence of an aneurysm of the left ventricle was established. His electrocardiogram on admission (Fig. 2,*A*) revealed deep Q waves in Leads I and IV, with a rather markedly elevated RS-T segment in Lead IV. The patient's course at this hospital was uneventful and he was discharged in December, 1942.

Because of epigastric cramps and belching the patient was readmitted in February, 1943. There was a moderately icteric tint to the sclerae on this admission and during his hospitalization he had at least two episodes of severe epigastric and precordial pain with low-grade fever, jaundice, leucocytosis, and rise in sedimentation rate. On Nov. 8, 1945, an acutely gangrenous gall bladder was excised and the patient made an uneventful recovery. In all his hospital records over a five-year period, the patient's electrocardiograms (Fig. 2,*A* and *B*) have exhibited similar abnormalities.

CASE 2.—W. H., a 57-year-old white man, was admitted to the neurological service in July, 1946, because of clonic convulsions and a period of unconsciousness. About one year prior to this admission he had suffered a cerebrovascular accident resulting in a right hemiplegia. X-ray examination of the patient's chest following the subsidence of convulsions was reported to exhibit a large mass in the region of the left ventricle, suggestive of a ventricular aneurysm. The patient was transferred to the medical service for further study where previous hypertension, cardiac, and renal disease were denied by him. Significant physical findings other than the residual neurological changes were limited to the cardiovascular system. The apex impulse was visible and palpable in the fourth and fifth intercostal spaces, 13.0 cm. from the midsternal line. Enlargement to the left was noted on percussion and the heart sounds were of fair quality and intensity. Kymographic, fluoroscopic, and x-ray examination (Fig. 3) confirmed the presence of ventricular aneurysm. An electrocardiogram on Aug. 13, 1946, (Fig. 4,*A*) exhibited Q waves and persistent RS-T segment elevations in Leads I and CF_4. The patient was discharged on Sept. 20, 1946, and has remained asymptomatic. In a follow-up electrocardiogram recorded on Sept. 4, 1947, (Fig. 4,*B*) no changes were noted when compared with previous tracings.

CASE 3.*—J. M., a 65-year-old white man, with a history of left hemiplegia of about twelve years' duration and exertional dyspnea of four years' duration, was admitted to another hospital because of severe precordial pain. Of interest was a report from that hospital noting a diffuse pulsation in the region of the fourth, fifth, and sixth intercostal spaces on the left, weak heart sounds over this area, and the presence of a ventricular aneurysm by x-ray films and cardiac fluoroscopy. His electrocardiograms at that time exhibited an absent R wave and an elevated RS-T segment in Lead CF_4. The patient was transferred to this hospital for convalescent care. His course here was uneventful. X-ray examination of the chest (Fig. 5) confirmed the presence of a ventricular aneurysm. On a repeat electrocardiogram (Fig. 6), persistence of the abnormal pattern was noted. The patient was discharged for out-patient care.

*Case previously reported by Crawford.[11]

Fig. 1.—Case 1. An aneurysmal bulge at the upper border of the left ventricular curve is present in this teleroentgenogram.

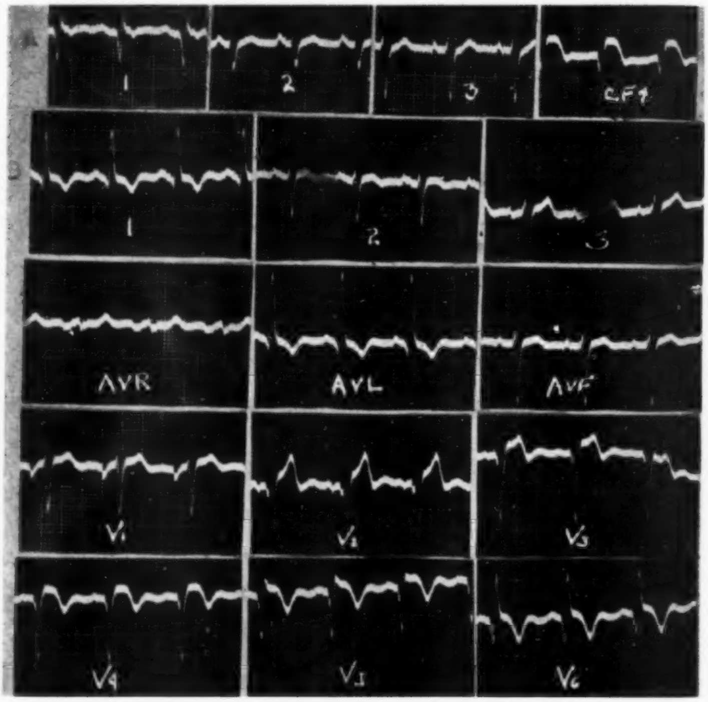

Fig. 2.—Case 1. *A*, Dec. 3, 1941. In Lead I deep Q waves and inverted T waves are present. In lead CF_4* prominent Q waves and elevated RS-T segments are present.

B, Sept. 9, 1947. In precordial Leads V_2 through V_6† persistence of Q waves and elevated RS-T segments are noted.

*CF_4 in all tracings is half standardized.

†V Leads in all tracings are fully standardized.

Fig. 3.—Case 2. A marked aneurysmal bulge at the upper border of the left ventricular curve is present in this teleroentgenogram.

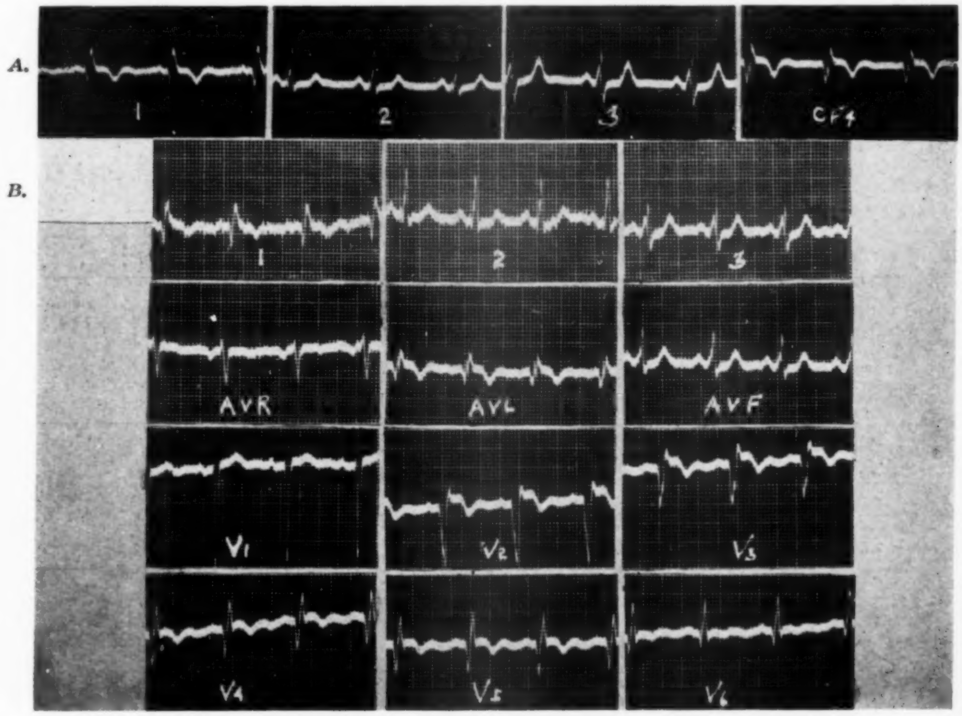

Fig. 4.—Case 2. *A*, Aug. 13, 1946. In Lead I deep Q waves and inverted T waves are present. In precordial Lead CF_4 there are noted deep Q waves, elevated RS-T segments, and inverted T waves.

B, Sept. 9, 1947. In Lead I the deep Q waves and inverted T waves are unchanged. In precordial leads persistent Q waves, elevated RS-T segments (V_2 through V_4) and inverted T waves (V_2 through V_6) are present.

CASE 4.—B. G., a 61-year-old white man, was admitted in July, 1942, for further treatment because of an unresolved pneumonia. About two years prior to admission he had been hospitalized because of myocardial infarction. On physical examination residual dullness and decreased fremitus below the right scapula, diminution of breath sounds over the same area, and crackling râles were noted. The heart was enlarged by percussion and an apical systolic murmur was heard. Examination was otherwise noncontributory. X-ray films of the chest (Fig. 7) revealed an aneurysm of the left ventricle, which was confirmed by fluoroscopic examination. His electrocardiogram (Fig. 8) exhibited a deep Q wave and an elevated RS-T segment with inverted T waves in Lead I. In a precordial lead, CF_4, a deep Q wave was present, the RS-T segments were elevated, and the T waves were inverted. The patient made an uneventful recovery from his pneumonia and was discharged to be followed up in the out-patient clinic.

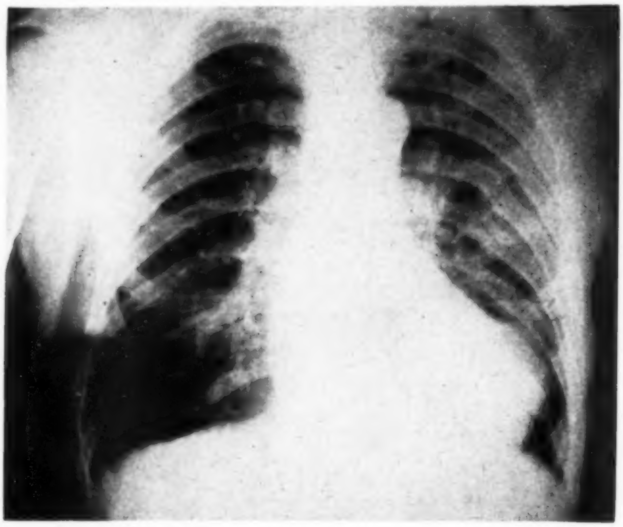

Fig. 5.—Case 3. An aneurysmal bulge at the midsegment of left ventricular curve is noted in this teleroentgenogram.

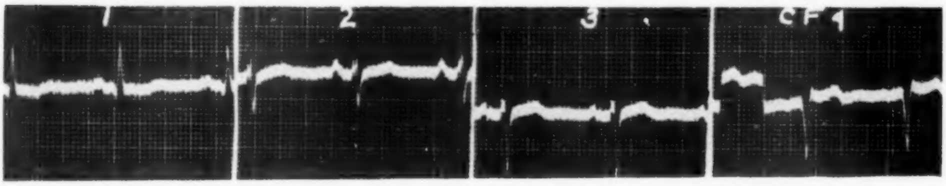

Fig. 6.—Case 3. May 16, 1942. In Lead I low T waves are present. In precordial Lead CF_4 deep Q waves and elevated RS-T segments are present.

CASE 5.—S. L., a 70-year-old white man, was transferred from another hospital to this hospital in November, 1943. He was known to have suffered from pernicious anemia for about two years. His cardiac symptoms were of about one year's duration; there had been two bouts of failure. No history of precordial pain could be elicited, but a diagnosis of old infarction of the anterior wall had been made at another hospital. Physical examination on admission to this hospital revealed a pale, chronically ill man. There was dullness at the base

of the right lung with moist râles over this area. The heart was enlarged by percussion, but otherwise not unusual. His blood pressure was recorded as 130/90. An x-ray film of the chest was reported to show productive changes at both apices and a small effusion at the base of the right lung; the heart was reported to be slightly enlarged. In electrocardiograms (Fig. 9,*A* and *B*) recorded on Feb. 14, 1944, and March 4, 1944, respectively, similar findings were noted. These consisted of Q waves and inverted T waves in Lead I and of deep Q waves with elevated RS-T segments and inverted T waves in Lead CF_4. Because of persistently low basal metabolic rates the patient was placed on thyroid therapy but showed little response to this medication. He died on July 8, 1944, about eight months after admission to this hospital, following an episode

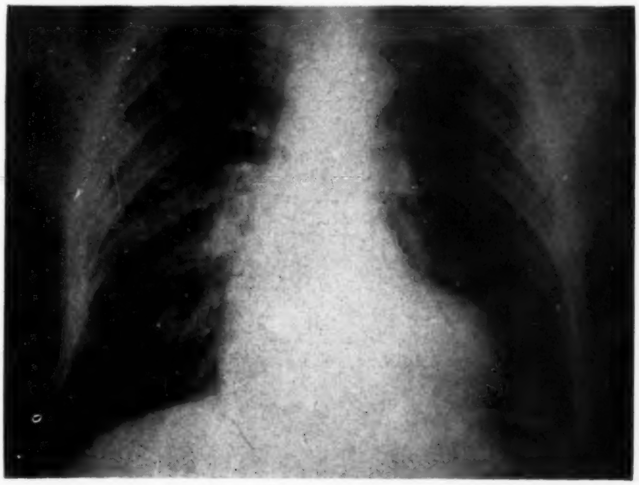

Fig. 7.—Case 4. Slight bulging of the upper left ventricular border is present in this teleroentgenogram. This was confirmed as a ventricular aneurysm by fluoroscopy and kymography.

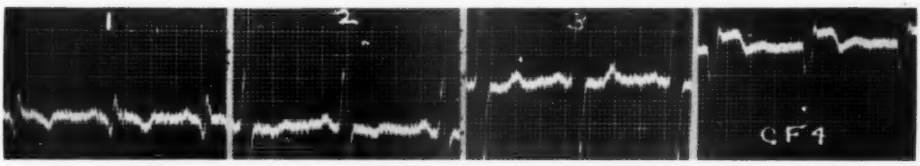

Fig. 8.—Case 4. July 3, 1942. In Lead I deep Q waves and inverted T waves are present. In Lead CF_4 prominent Q waves and elevated RS-T segments are noted.

of acute left ventricular failure. Post-mortem examination revealed a heart that weighed 420 grams. The lower one-third of the interventricular septum and part of the anterior wall of the left ventricle was the site of a ventricular aneurysm. The coronary arteries were markedly narrowed by atheromatous plaques and calcific deposits, and there was a partial occlusion of the left coronary artery by an old thrombus. The lungs contained bilateral apical fibrocaseous tuberculosis with bronchogenic spread to all lobes.

CASE 6.—E. F., an 82-year-old white man, was admitted to this hospital on May 3, 1946, because of pain and swelling of the fourth right toe of one week's duration. In addition, he gave a history of retrosternal pain, fleeting in nature and not related to exertion. There was no history of ankle edema or exertional dyspnea. Upon examination his temperature

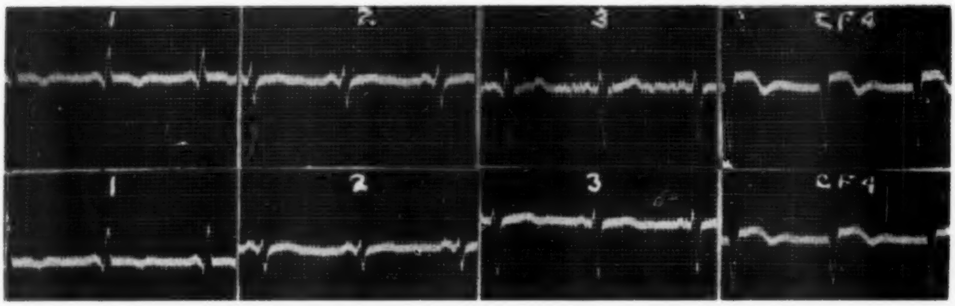

Fig. 9.—Case 5. *A*, Feb. 12, 1944. Prominent Q waves and inverted T waves are present in Lead I. In precordial Lead CF_4 deep Q waves, elevated RS-T segments, and inverted T waves are present.

B, March 4, 1944. Leads I and CF_4 are unchanged when compared with previous tracing. Ventricular aneurysm was confirmed by autopsy.

was noted to be 101° F., his pulse 90 beats per minute, his respiratory rate 26 per minute, and his blood pressure 100/54. The lungs were hyperresonant to percussion except over the left upper lobe anteriorly and posteriorly. The heart was not enlarged, the sounds were of fair quality, and the rhythm was regular. A rough systolic murmur was heard over the aortic area. The extremities exhibited marked sclerosis of the peripheral vessels and the fourth right toe was swollen, red, warm, and tender. An x-ray film of the chest was interpreted as exhibiting the findings of incomplete consolidation involving the left lower lobe as well as the right middle and right lower lung fields. An electrocardiogram (Fig. 10) exhibited a Q wave, a small R wave,

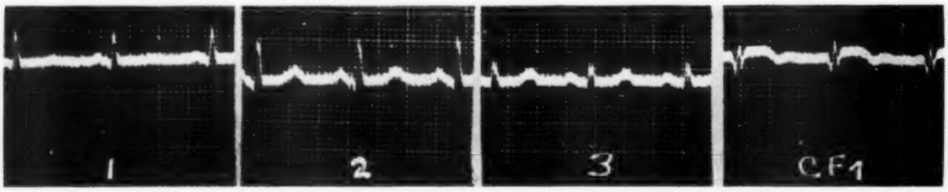

Fig. 10.—Case 6. May 6, 1946. In Lead I isoelectric T waves are present. In Lead CF_4 prominent Q waves, elevated RS-T segments, and inverted T waves are present. Ventricular aneurysm was confirmed by autopsy.

elevated RS-T segment, and an inverted T wave in Lead CF_4. The patient's peripheral vascular disease responded to paravertebral blocks and conservative therapy. Most of his work-up was directed at evaluation of the lung pathology since it was felt that the patient probably suffered from a carcinoma of the lung. The patient's cardiac status remained fairly good. He expired on Nov. 6, 1944, about six months after admission. Post-mortem examination revealed tuberculosis of left upper and left lower lobes of the lungs. The heart weighed 390 grams. In the anterior wall of the left ventricle adjacent to the middle portion of the interventricular septum there was an aneurysmal dilatation of the wall. The aneurysm was composed of fibrous tissue and measured 5.0 cm. in diameter. The left descending coronary artery was markedly narrowed by atherosclerosis and occluded by a calcified thrombus for a distance of one centimeter.

CASE 7.—C. V., a 61-year-old white man, was transferred from another hospital in March, 1943, with a two-year history of ankle edema, dyspnea, orthopnea, and paroxysmal nocturnal dyspnea which had necessitated many hospitalizations. On admission to this hospital he was found to have an enlarged heart, an enlarged liver, and ankle edema.

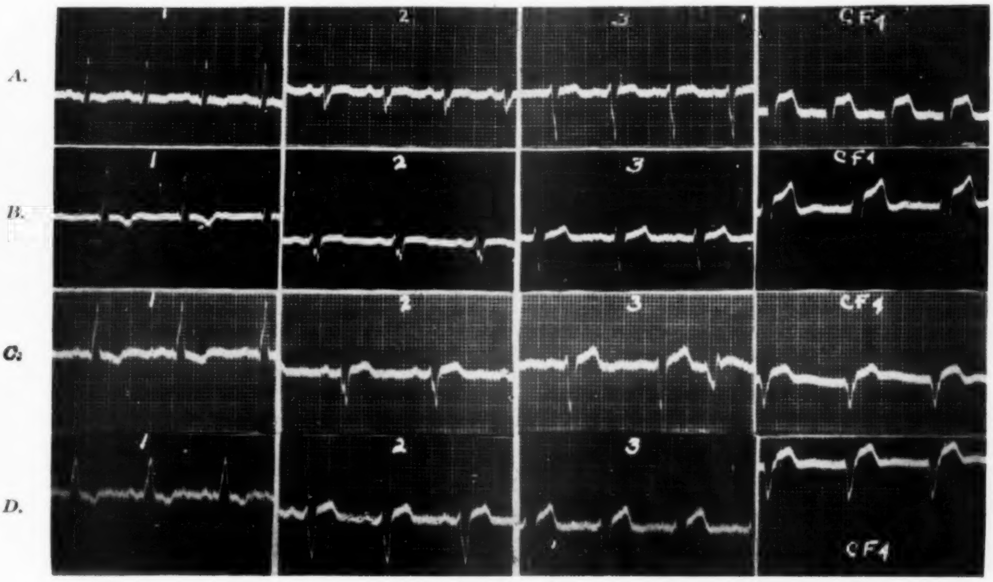

Fig. 11.—Case 7. *A*, March 1, 1943. In Lead I there are inverted T waves. In precordial Lead CF_4 deep Q waves and markedly elevated RS-T segments are present.

B, May 7, 1943. In Lead I there are small Q waves and inverted T waves. In precordial Lead CF_4 small R waves and markedly elevated RS-T segments are noted.

C, Oct. 31, 1945. Lead I is unchanged when compared with previous tracing. In Lead CF_4 deep Q waves and elevated RS-T segments are present.

D, Jan. 30, 1947. Lead I and precordial Lead CF_4 are unchanged when compared with previous tracing. Autopsy confirmed aneurysm of the left ventricle.

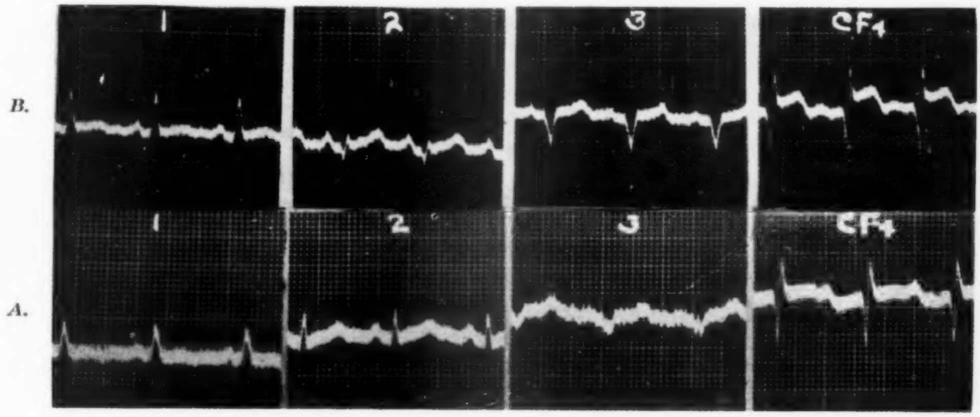

Fig. 12.—Case 8. *A*, May 2, 1947. In Lead I low upright T waves are noted. In precordial Lead CF_4 deep Q waves and markedly elevated RS-T segments are noted.

B, May 9, 1947. Lead I and precordial Lead CF_4 are essentially unchanged when compared with the previous tracing. Aneurysm of the left ventricle was confirmed by autopsy.

X-ray films revealed a pleural effusion on the right and a prominence of the left ventricular border. An electrocardiogram (Fig. 11,*A*) on March 1, 1943, exhibited a deep Q wave and markedly elevated RS-T segment in Lead CF_4. After thoracentesis the patient was maintained on digitalis and ammonium chloride without incident until April 1, 1943, when he suffered a cerebrovascular accident resulting in right spastic hemiparesis. He recovered sufficiently to become ambulatory on the ward. In April, 1947, about four years after admission, the patient suddenly collapsed, became comatose, and died on the same day. All electrocardiograms (Fig. 11,*B*, *C*, and *D*) taken while the patient was in this hospital, the last one having been recorded on Jan. 30, 1947, remained essentially unchanged. At post-mortem examination a small aneurysmal dilatation approximately 3.0 to 3.5 cm. in diameter at the apex of the left ventricle was found. Both the left and right coronary arteries showed old atherosclerotic occlusions.

CASE 8.—M. W., a 69-year-old Negro woman, was admitted to this hospital in April, 1947, with a history of diabetes mellitus of nine years' duration, hypertension for eight years, and a cerebrovascular accident about two years prior to admission, which resulted in a right hemiparesis. In July, 1946, the patient suffered another stroke involving the right side of the body. On her admission to this hospital, the abnormal findings were the presence of a fusiform pulsating mass in the abdomen thought to be compatible with an aneurysm of the aorta and a right spastic hemiparesis. An x-ray film of the chest was reported to be normal except for a dilated aorta. An electrocardiogram (Fig. 12,*A*) exhibited a deep Q wave and an elevated RS-T segment in Lead CF_4. Repeated tracings (Fig. 12*B*) showed no change. On May 9, 1947, the patient had a sudden onset of pain in the lower abdomen accompanied by vomiting, fall in blood pressure, and the appearance of a mass in the left lower quadrant. Despite blood and plasma transfusions she died on May 11, 1947. At post-mortem examination an aneurysm with thrombus formation in the iliac arteries and hemoperitoneum secondary to rupture of the left internal iliac artery were demonstrated. The heart weighed 275 grams. The greater part of the anterior wall of the left ventricle was very thin and fibrotic and presented the appearance of an extensive ventricular aneurysm. The anterior descending branch of the left coronary artery showed a grayish brown plaque which almost entirely occluded the vessel about 1.0 cm. from its orifice. About 0.5 cm. below this narrowing there was a complete occlusion of this vessel. This vessel supplied the area of a large, old infarct.

DISCUSSION

In eight patients suspected clinically of having ventricular aneurysm, roentgenographic and kymographic confirmation was obtained in four, and in the remaining four there was post-mortem confirmation. In the eight patients in whom cardiac aneurysm was thus proved, the electrocardiographic features noted in all instances were the presence of Q waves and persistent elevation of the RS-T segments in the precordial leads over the septal area and left side of the heart. In addition, the RS-T segments in the precordial leads remained elevated and tended to exhibit an upward convexity after the intital evidence of myocardial infarction had subsided. The T waves were diphasic or inverted in all cases.

Although the limb leads in these cases frequently exhibited the changes of old infarction of the anterior wall, there were two patients (Cases 6 and 8) in whom these leads were lacking in changes significant of infarction, recent or old. However, the precordial leads in these instances exhibited the characteristic Q wave and RS-T segment elevation pattern. Contrary to the findings mentioned by Gross and Schwedel,[10] right axis deviation did not occur in any of our cases.

In four patients (Cases 2, 4, 5, and 7), the QRS complex was prolonged from 0.10 to 0.12 second. In patients with definite bundle branch block (QRS

greater than 0.12 second), the persistence of RS-T segment elevation in precordial leads does not, of course, have the same significance.

When the case histories of three additional patients whose necropsy records indicated cardiac aneurysm were reviewed, it was found that the electrocardiographic pattern which we have described was not present in the single CF_4 lead recorded in the charts. It is not correct, therefore, to infer that in all instances of cardiac aneurysm one will find the electrocardiographic changes which we have described.

In an effort to understand the mechanism responsible for persistent RS-T segment elevation we turned to both the clinical and experimental literature for aid. Suffice it to say that a reasonable explanation for persistent RS-T segment elevations was not apparent.

SUMMARY

1. The case histories and findings of eight patients with proved cardiac aneurysms are described.

2. Q waves and the persistent elevation of the RS-T segments in the precordial leads were the essential electrocardiographic findings in all eight patients. It is also true that of seven patients with necropsy findings of ventricular aneurysm, three did not show the persistent RS-T elevation in the precordial leads.

3. Present concepts of electrophysiology do not explain the persistence of elevated RS-T segments in cases of cardiac aneurysm.

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Clinical Reports

UNUSUAL CARDIAC ARRHYTHMIAS IN A PATIENT RECOVERING FROM SHOP TYPHUS

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WHILE recovering from shop typhus, a 17-year-old Javanese boy developed certain unusual arrhythmias. These will be described and discussed.

CASE REPORT

The patient was admitted to the Petronella Hospital at Jogjakarta at the end of December, 1940, because of a febrile illness. The fever subsided after one week. As his serum gave a positive agglutination with Proteus OX 19 (1:800), a clinical diagnosis of shop typhus was made. Shop typhus, a form of murine typhus, is observed rather often in Java.

During his illness it had been noted that his pulse was sometimes irregular and slow. This persisted during convalescence, during which period I had the opportunity of studying the case. When I first saw the patient on Jan. 7, 1941, his pulse was slow and not quite regular. Otherwise the physical examination was essentially negative. The heart was not enlarged and the heart sounds were of normal quality. Roentgen examination of the chest showed a normal heart shadow.

In the following weeks the patient felt entirely well, but his pulse was often irregular and usually slow. Many electrocardiograms were taken. After about two months the patient was discharged and resumed his work in an office. He was highly interested in his pulse abnormalities and on my request kept a daily record of his observations. During 1941 and 1942 his pulse remained abnormal. As a result of the Japanese occupation it became difficult to keep in contact with the boy. The last time I saw him was in April, 1943, his pulse then being still very slow and irregular. Up to this date the young man had remained in excellent health and carried out his duties as usual.

Electrocardiograms.—The electrocardiograms (taken with a Sanborn Cardiette) varied from day to day, and sometimes from hour to hour. The records will not be presented chronologically, but the less complicated ones will be given first.

An electrocardiogram made on Feb. 1, 1941 (Fig. 1) shows sinus rhythm with a rate of approximately 60 per minute. P-R conduction time is 0.16 second. The contour of the P wave is abnormal; P_1 is notched, P_2 very small and diphasic, and P_3 negative and notched.

An electrocardiogram made on Feb. 22, 1941 (Fig. 2) shows sinus rhythm with a rate of 56 per minute. P-R conduction time is 0.14 second. Again the

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Received for publication Jan. 19, 1948.

P-wave pattern is abnormal, but it differs from that shown in Fig. 1. P_2 and P_3 are now diphasic with a pointed inverted component.

Another record, an electrocardiogram made on Feb. 3, 1941 (Fig. 3), again shows an abnormal P-wave pattern. P_1 is small and diphasic, P_2 diphasic with a sharp inverted component, and P_3 diphasic. P-R conduction time is 0.12 second. The heart rate is only 40 per minute.

In these three tracings the P-wave contour is definitely abnormal, indicating a location of the pacemaker in an unusual site of the sinus node or an abnormal spread of the stimulus through the auricles, or both.

In Fig. 1 the P-R interval is normal; obviously the heart beat originates in the head of the node. The slower rhythm and shorter P-R interval present in Fig. 2 indicate that the pacemaker is in a lower part of the node. The slow rate and short conduction time seen in Fig. 3 suggest a rhythm arising in the tail of the sinus node. The possibility of an upper nodal rhythm in this last record is refuted by the following arguments:

1. In retrograde excitation of the auricles a definite pattern of the retrograde P wave is obtained; such a wave is inverted in Leads II and III, and may be upright or diphasic in Lead I.[1,2]

2. The P-R interval in this record is more than 0.10 second. However, in some cases of A-V nodal rhythm with A-V block, the P-R interval may be over 0.12 second.[3]

3. In other records made on this patient which show interference or intermittent dissociation (vide infra), the same P-wave pattern was sometimes present.

Lead III of a tracing made on Feb. 1, 1941 (Fig. 4,*A*) shows sinoauricular block. This disturbance was often observed; sometimes block occurred every third or fourth beat, but more often it occurred irregularly. Only occasionally were two successive sinus beats blocked (Fig. 4,*B*).

Accurate measurement reveals that the P-P interval bounding a pause is a trifle less than two or three times the normal P-P interval. Perhaps this is due to the so-called Weckebach phenomenon in S-A block.[4]

S-A block was observed only when the heart rhythm was controlled by the same pacemaker that was acting in the tracing shown in Fig. 1.

In Lead III of a tracing made on March 12, 1941 (Fig. 5), the same pacemaker which is acting in the tracing shown in Fig. 4,*A* is responsible for the second, fifth, and sixth beats. Obviously there exists S-A block. In the pauses, a lower center in the sinus node escapes. The rate of the two pacemakers is 77 and 45 per minute, respectively.

Lead I of a tracing made on March 12, 1941 (Fig. 6), shows complex arrhythmia to be present. In the first, fifth, eighth, ninth, tenth, and eleventh beats the same sinus pacemaker which is acting in the tracings shown in previous figures is easily recognized. The P wave in the ascending limb of the T wave in the second beat is definitely of the same origin. The intervals between the several P waves of this pacemaker are multiples of a common divisor: 0.76 or 0.77 second. This is the inherent rhythm of this center as is shown in the succession of two of its beats (eighth and ninth beats).

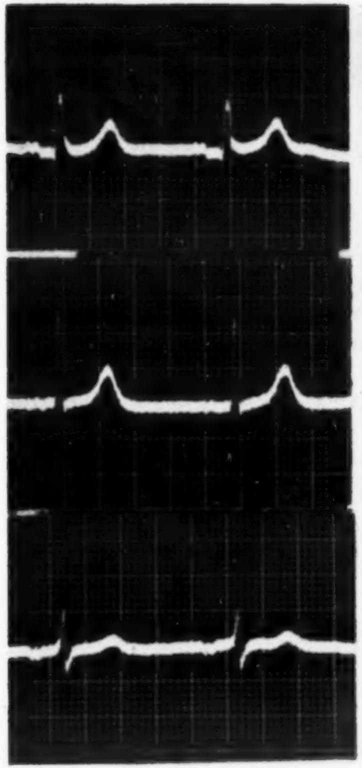


Fig. 1.

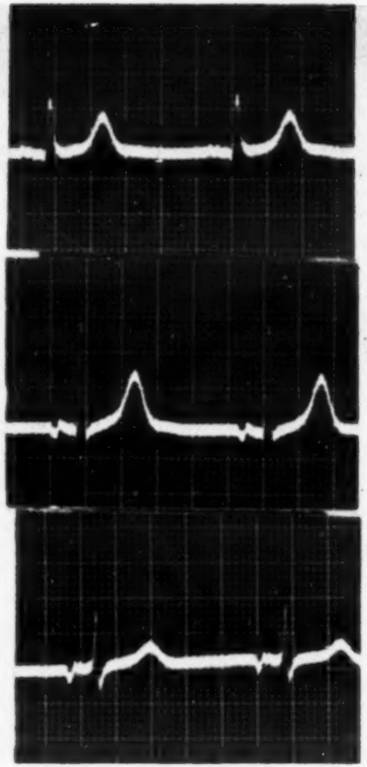


Fig. 2.

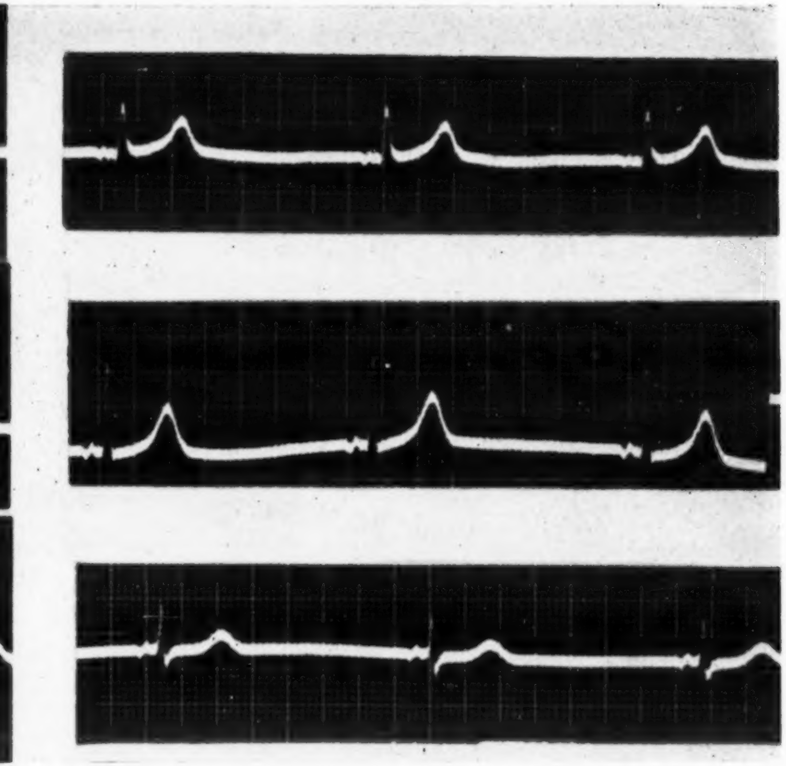


Fig. 3.

Fig. 1.—Feb. 1, 1941. Sinus rhythm, rate 60. P-R interval 0.16 second. P_1 notched, P_2 small, and P_3 negative and notched.
Fig. 2.—Feb. 22, 1941. Sinus rhythm, rate 56. P-R interval 0.14 second. P_2 and P_3 diphasic with a pointed inverted component.
Fig. 3.—Feb. 3, 1941. Sinus rhythm, rate 40. P-R interval 0.12 second. P_1 diphasic, P_2 diphasic with a sharp inverted component, and P_3 diphasic.

A.

B.

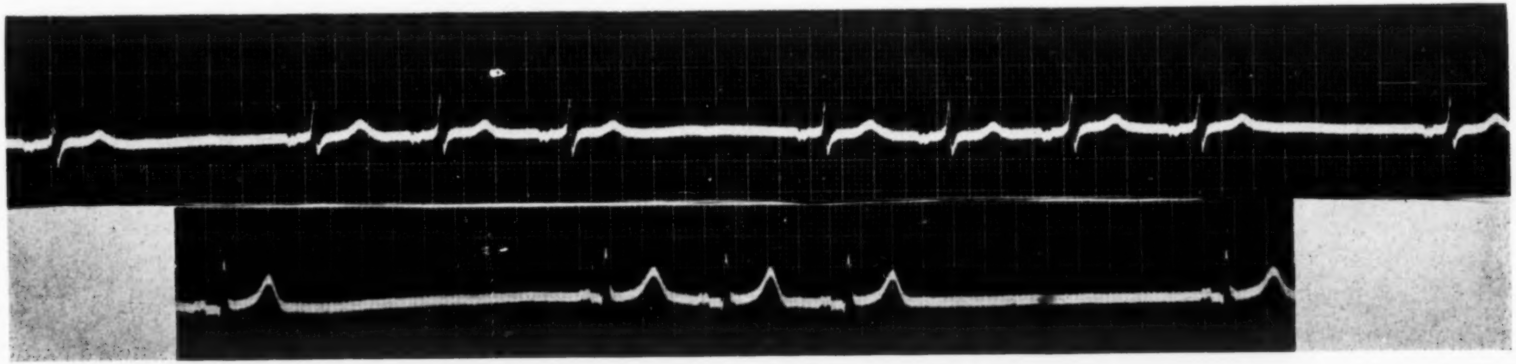


Fig. 4.—*A*, Feb. 1, 1941. Lead III. S-A block. *B*, March 12, 1941. Lead I. S-A block.

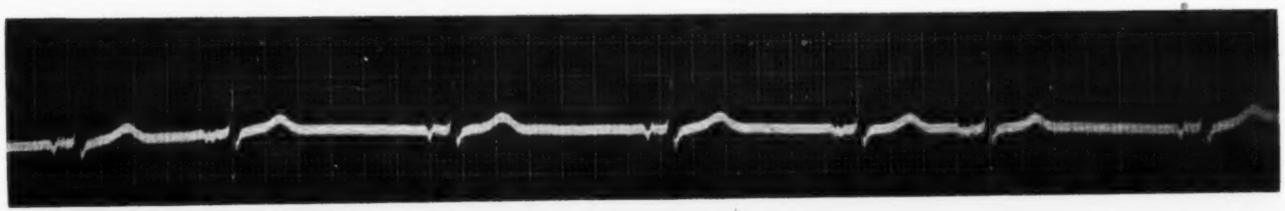


Fig. 5.—March 12, 1941. Lead III. S-A block with escape of a lower pacemaker in the S-A node.

After the first beat, S-A block develops. The second beat is a nodal escape with a sinus P wave in the T wave; this sinus impulse fails to reach the ventricles as a result of the refractory state of the junctional tissues (interference). The third and fourth beats originate in a lower part of the sinus node (probably at the same site that was acting in the tracing shown in Fig. 2). It is very remarkable that this center should escape *after* the nodal pacemaker. This same center operates in the sixth and seventh beats, its rate being 46 per minute. In this record, therefore, three pacemakers are present. The highest center discharges the lower pacemakers, but the reverse is not true.

In Lead III of a tracing made on April 10, 1941 (Fig. 7), the two pacemakers in the sinus node are operating alternately. Perhaps the alternate impulses from the higher center are prevented from reaching the auricles (S-A block). In the pause which follows, the lower center escapes and an unusual form of ventricular bigeminy results.

In Lead III of a tracing made on Feb. 8, 1941 (Fig. 8), there are two pacemakers active: one is in the A-V node, the other in the sinus node. The first four beats are of nodal origin, but the control of the auricles is in the sinus node. Both rhythms are irregular and slow. The fifth beat is a conducted sinus beat. The QRS complex of this beat differs from the QRS complex of a nodal beat. This record, therefore, is an instance of ***intermittent dissociation***. Interference and dissociation were often observed in this patient.

Limb leads and Lead CR_4 of a tracing made on Jan. 7, 1941, are reproduced in Fig. 9. This tracing shows A-V dissociation; the ventricular beats are of nodal origin, but the auricles are under the control of the sinus node. The P wave is abnormal. The P-P interval is rather constant, corresponding to a rate of 46 to 47 per minute. The ventricular complexes, however, show irregular spacing; furthermore, this irregularity is definitely periodic. The shorter R-R intervals are almost identical in each lead and equivalent to a rate of 48 to 49 per minute. The QRS to P interval varies in every beat; it lengthens in every successive cycle. When this interval becomes more than 0.19 second, a long R-R interval invariably follows. These longer R-R intervals vary between 1.44 and 1.50 seconds.

Comment on Fig. 9.—Presumably, the explanation is as follows: As in most cases of complete A-V dissociation, the sinus pacemaker discharges impulses at a rate only slightly slower than the rate of the nodal pacemaker. Up to the point at which a longer R-R interval occurs, the sinus impulse arrives at the A-V junction when it is still in its refractory state. Since the sinus rate is slower, the successive sinus stimuli arrive later and later in the refractory phase of the A-V junction. Eventually the sinus impulse comes so much later that it is able to penetrate into the nodal pacemaker and to suppress it. However, this impulse is prevented from passing into the ventricles because the A-V junction below the nodal pacemaker is still refractory, or perhaps abnormally depressed. Then the sinus impulse is ***blocked*** from passing into the ventricles. The nodal pacemaker can rebuild and discharge an impulse again before another sinus impulse can reach it.

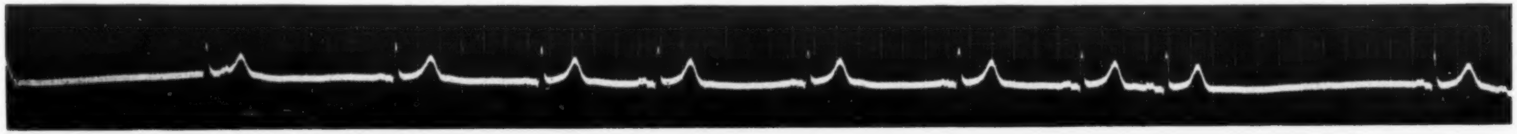
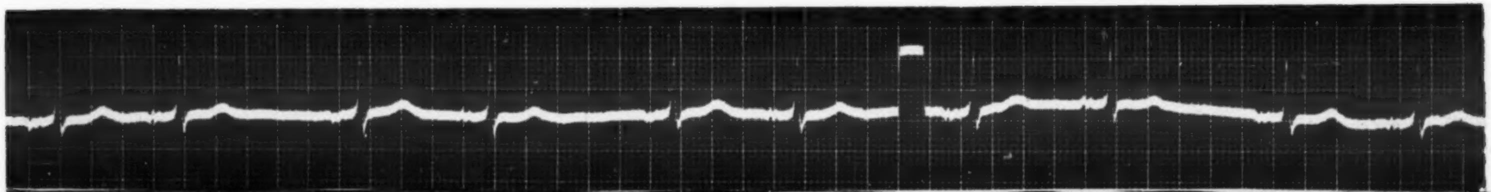


Fig. 6.—March 12, 1941. Lead I. S-A block with escape of lower centers. Three pacemakers are operating.

Fig. 7.



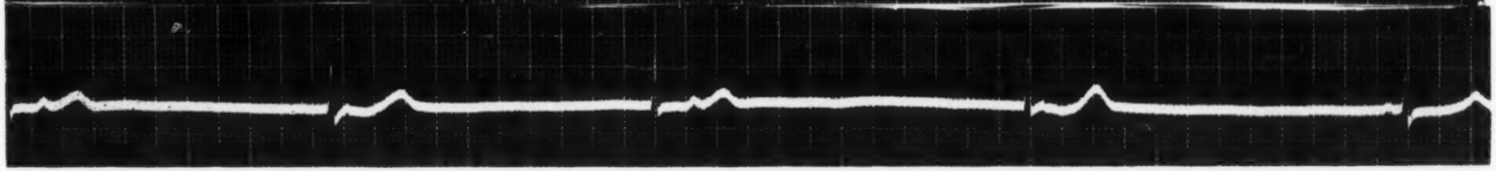


Fig. 8.

Fig. 7.—April 10, 1941. Lead III. Unusual form of ventricular bigeminy.

Fig. 8.—Feb. 8, 1941. Lead III. Intermittent dissociation. Both rhythms are irregular and slow.

I

II

III

IV_R

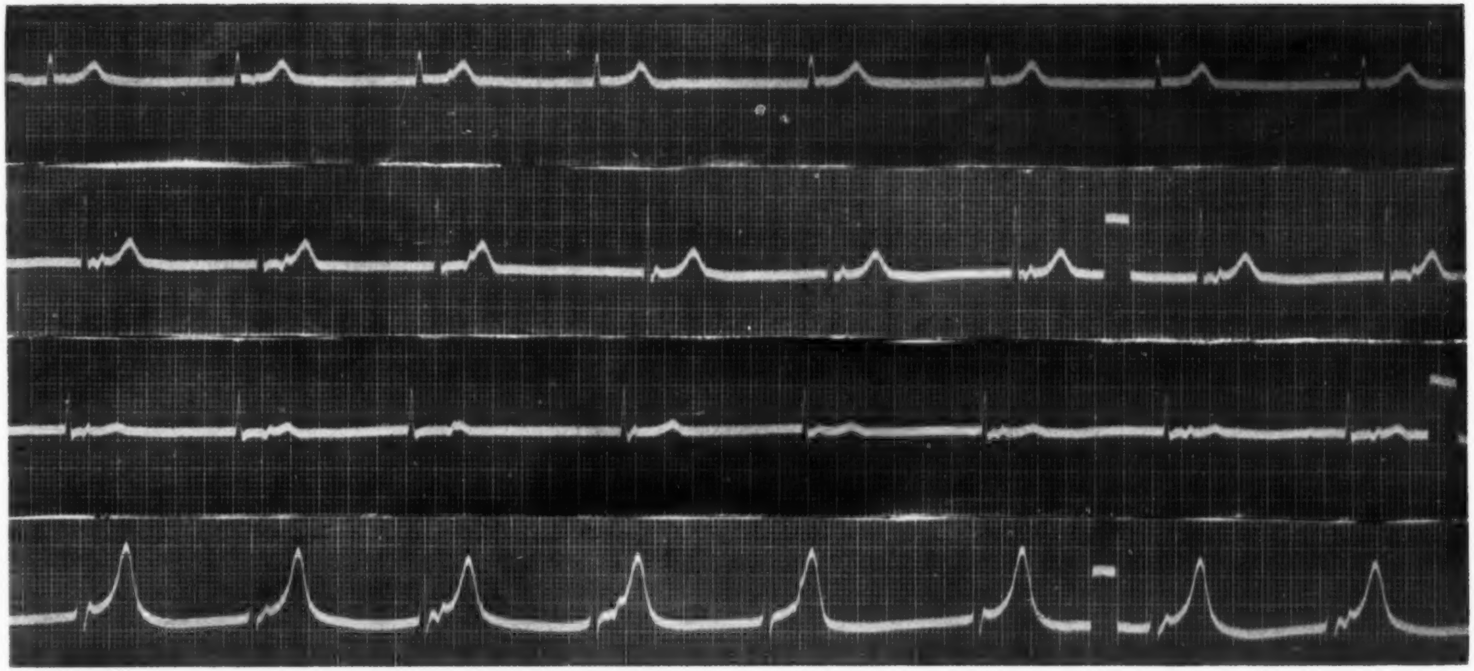


Fig. 9.—Jan. 7, 1941. Three limb leads and Lead IV_R (in the latter the top of the R goes off the record). An unusual form of complete A-V dissociation.

Therefore, in this record an unusual form of complete A-V dissociation is present. In the literature similar records are rare, but examples have been described by Langendorf and Katz.[5] It is one form of what Langendorf[6] has called "concealed conduction."

This unusual form of complete A-V dissociation was often observed in this patient. Sometimes the ventricular pause occurred after many beats, sometimes after every fourth or every third beat. On one occasion it was recorded after every second beat (Fig. 10). An uncommon type of ventricular bigeminy results.

A tracing made on Jan. 8, 1941 (Fig. 11), is a continuous record of Lead II, except that between the first and second strips a small portion is omitted. The first and second strips show a pseudoreciprocal rhythm and intermittent dissociation. The P-R distance in the conducted beats varies from 0.14 to 0.20 second; the conduction is aberrant. The third beat of the third strip is a conducted sinus impulse; the QRS complex of this beat differs slightly from that of a nodal beat. After the fourth beat in the third strip and in the fourth and fifth strips, groups of three beats occur, separated by long pauses. The longest pause lasts 4.6 seconds. The first and second beats of each triplet are of nodal origin. The R-R interval of these beats varies from 0.83 to 0.98 second. The third beat of each triplet is preceded by a negative P; the P-R interval of these cycles varies from 0.12 to 0.08 second. The R-R interval between the second and third beats of a triplet varies from 0.70 to 0.89 second. The origin of this third beat is not clear. It is notable that the long pauses appear after this third beat. Every long pause (with auricular and ventricular standstill) is terminated by escape of the nodal center; this pacemaker is regularly suppressed by this third beat. Perhaps this points to an origin of this third beat above the nodal pacemaker. It is noteworthy that during a long pause ventricular escape never was observed to occur.

Electrocardiograms made on Feb. 11, 1941, are reproduced in Fig. 12. *A* shows a rare form of ventricular bigeminy. The first beat of each couplet is of nodal origin. Each nodal beat is coupled with a supraventricular beat since an auricular complex is present between each pair of successive beats. The coupling is fairly fixed: the interval between two successive beats varies from 0.64 to 0.68 second. Therefore, this is an example of a dominant atrionodal rhythm with ventricular bigeminy and an intervening P wave. Couplets in Lead II are shown in Fig. 12,*B* and *C*; in Lead III, in Fig. 12,*D*. This bigeminy continued for a long time.

A further study of the couplets in the several leads reveals the following: (a) The R-R interval of the nodal beats varies between 2.74 and 2.96 seconds. (b) Notwithstanding this slight variation in the dominant rhythm, the coupling remains fixed (0.64 to 0.68 second). (c) The P wave is small and diphasic in Lead I and inverted in Lead III. It varies in Lead II (compare 12,*B* and 12,*C*) but is negative in most couplets of this lead.

Comment on Fig. 12.—The interpretation of records similar to those shown in Fig. 12 is often difficult. The subject has been amply reviewed by Perelman

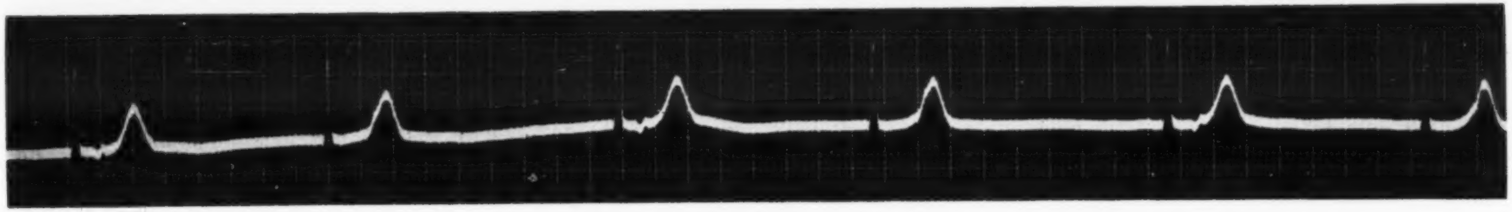


Fig. 10.

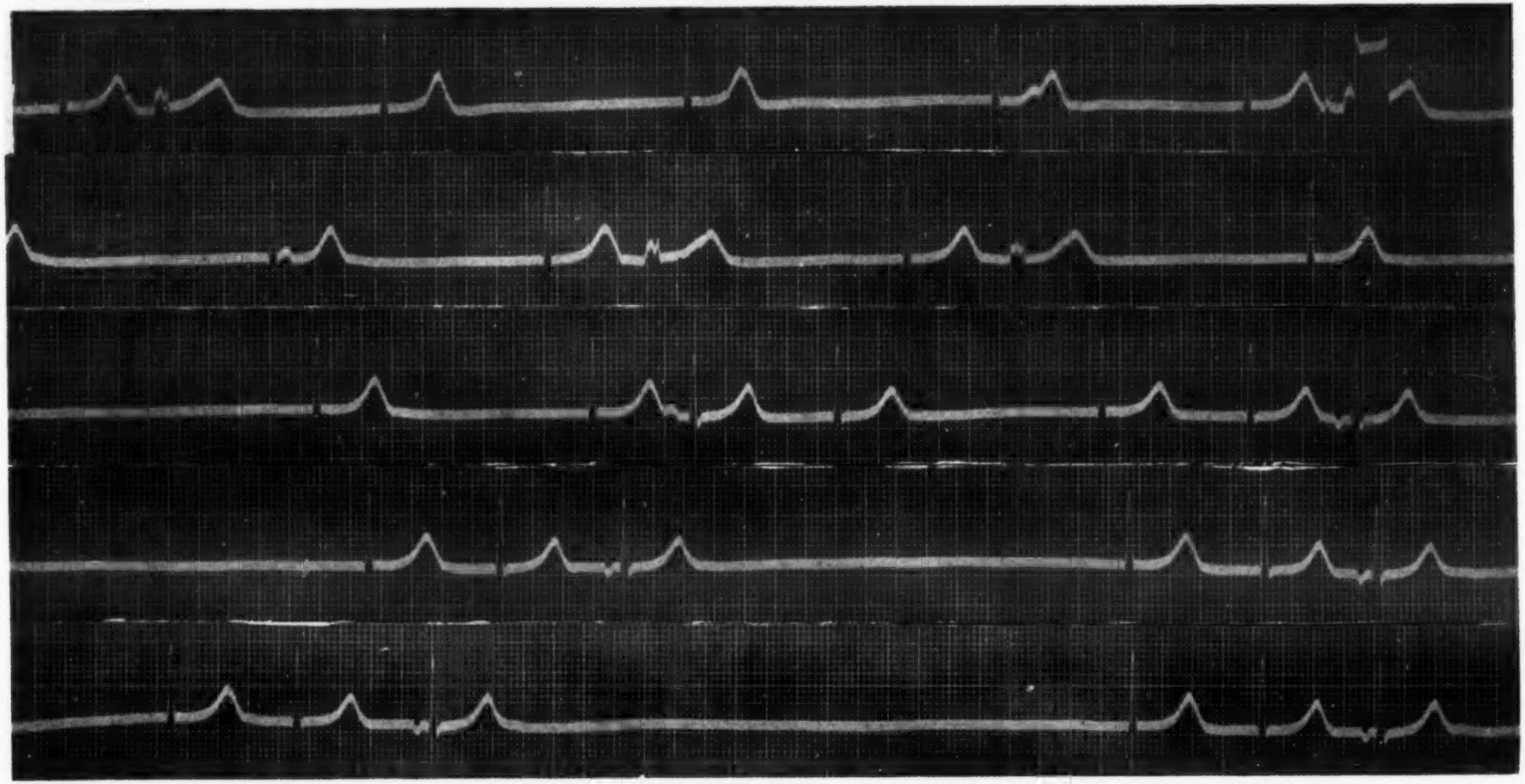
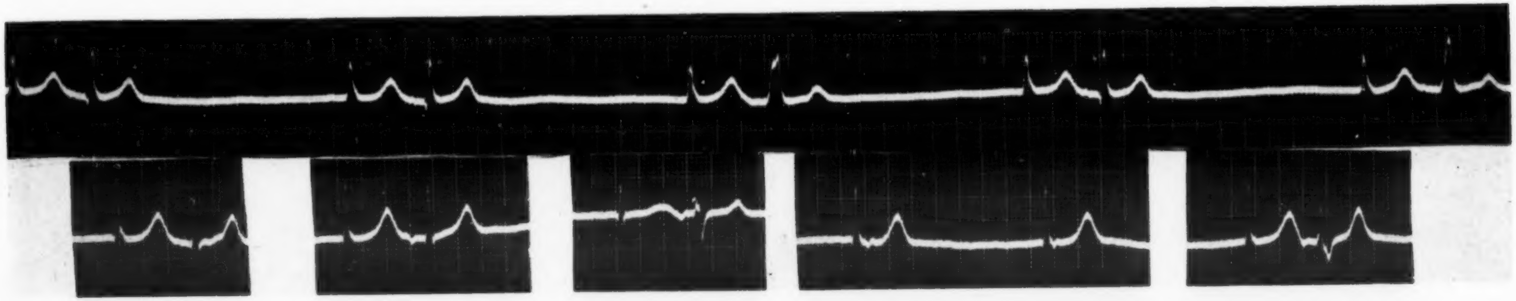


Fig. 11.

Fig. 10.—An uncommon type of ventricular bigeminy in an unusual form of complete A-V dissociation.

A.



B. C. D. E. F.

Fig. 12.—Feb. 11, 1941. *A*, Lead I. Dominant atrionodal rhythm with ventricular bigeminy and an intervening P wave. Discussed in text.

and Miller.[7] They discuss several possibilities which might explain the mechanism of this arrhythmia. They clearly point out that a study of the mode of onset and/or termination of the bigeminy is of paramount importance for the explanation of the mechanism involved. Fortunately in this case the mode of onset was recorded. At the onset nodal rhythm is present with interference and intermittent dissociation (Fig. 12,*E* and *F*). The R-R interval of the nodal beats varies from 1.52 to 1.60 seconds. The P waves of the sinus rhythm are abnormally shaped (as in previous curves). The sinus impulse only occasionally passes through to the ventricles, and when it does conduction is aberrant (Fig. 12,*F*).

Both pacemakers gradually slowed down. Obviously, for some reason, the automatic centers became markedly depressed. This is an important feature for the understanding of this record. Then suddenly the ventricular bigeminy with fixed coupling appeared.

As stated already, the coupling between the two beats was fixed notwithstanding slight variations in the R-R interval of the dominant nodal rhythm. This is a serious objection to the assumption that two independent rhythms exist, because it is illogical to assume that the sinoauricular pacemaker would show the same slight variations in rate that the nodal center shows. Therefore, in one way or another, the second beat of the couplet must be dependent upon the first and therefore related to it.

The pattern of the intervening P waves might point to their nodal origin. It is, however, unlikely that this is an instance of reciprocal rhythm because: (a) An inverted P wave was often observed in this patient when a sinus pacemaker controlled the heart. (b) Reciprocal rhythm should be diagnosed only when the P wave between the two ventricular beats differs considerably from the sinus P waves.[8] (c) The R-P interval is 0.52 second, which would be very long for retrograde conduction.

If a reciprocal rhythm can be excluded, perhaps the mechanical theory might be turned to for an explanation. Perelman and Miller[7] point out that most authors reject the theory of a direct mechanical stimulation, there being no evidence that the contraction of the ventricles in itself constitutes a proper stimulus for an auricular systole. However, there remains a possibility that a rise in intra-auricular tension may stimulate the auricular pacemaker.[9] This conception offers a possible explanation of the relation between the coupled beats in Fig. 12. At the time of the couplets the sinus pacemaker was markedly depressed, but the nodal center was depressed also. At the end of a long pause the ventricles (and perhaps the auricles, too) were overfilled with blood. Eventually the nodal pacemaker discharged: during the contraction of the ventricles a sharp rise in the intra-auricular tension could result and this might conceivably cause the sinus pacemaker to discharge.

The difference between the coupling in Fig. 12,*F* and in Fig. 12,*A*, *B*, *C*, and *D* must be emphasized. In Fig. 12,*F* the discharge of the sinus pacemaker is automatic; this coupling is not fixed. In the remaining tracings of Fig. 12, coupling is fixed; the second beat of the couplet is therefore dependent upon the first beat. Sudden rise of the intra-auricular pressure is at least a possible

explanation of the discharge of the suppressed pacemaker by the first beat of the couplet. Unfortunately, the termination of the bigeminy was not recorded.

Such a persistent type of atrionodal rhythm with ventricular bigeminy is very unusual. A case reported by Perelman and Miller has been referred to.

Influence of Exercise.—The influence of exercise on the heart rhythm was studied on several occasions. In a tracing made Feb. 22, 1941, with the patient at rest, there was a sinus rhythm with a rate of 60 per minute. Records were then taken immediately and some minutes after the patient had sat up and had lain down twenty times. No acceleration occurred; the rate of the same pacemaker remained 60 per minute. A second exercise test on the same day yielded another result. After exercise the command of the heart was taken over by a faster pacemaker in the sinus node; however, pauses appeared repeatedly (S-A block) and the original pacemaker soon regained the control of the heart rhythm.

From these and similar tests it was evident that the rate of a given pacemaker could scarcely be influenced by exertion. Likewise, no influence on the heart rate could be detected by a subcutaneous injection of 0.5 mg. of atropine sulfate.

DISCUSSION

In the many records of this patient, taken during a period of considerable duration, the rhythm-producing function was almost never located in the normal pacemaker of the heart. The control of the heart was taken over by the other automatic centers situated in a lower part of the S-A node and the A-V node. The function of these lower pacemakers was seriously damaged also.

Commonly, such an excessive and permanent depression of the function of the automatic centers is caused by organic disease. As this patient was recovering from shop typhus, the possibility exists that the nutritional arteries of the pacemakers of the heart were the seat of a thromboarteritis, caused by ***Rickettsia mooseri***. No further proof for this conception can be given. Perhaps the arrhythmias were purely coincidental.

No symptoms or signs of a widespread myocardial lesion were present. Up to April, 1943, the pulse of the patient remained slow and irregular. His ultimate fate is not known.

SUMMARY

Unusual cardiac arrhythmias are described which were observed in a 17-year-old Javanese boy who was recovering from shop typhus. Among the arrhythmias analyzed are instances of S-A block (Figs. 4, 5, and 6), intermittent dissociation (Fig. 8), an unusual form of complete A-V dissociation (Figs. 9 and 10), pseudo-reciprocal rhythm and intermittent dissociation (Fig. 11), and dominant atrionodal rhythm with ventricular bigeminy and an intervening P wave (Fig. 12). Unusual forms of ventricular bigeminy are shown in Figs. 7, 10, and 12.

In the many records of this patient, taken during a period of many months, the rhythm-producing function was almost never located in the normal pacemaker

of the heart. Usually, centers in the lower part of the S-A node and the A-V node controlled the heart. However, the function of these centers was seriously affected also.

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HEMANGIO-ENDOTHELIOBLASTOMA OF THE HEART

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THE following case of a cardiac tumor is presented, first, because of its rarity and second, because it presents a fairly typical picture of the effects of such a lesion. To date some two hundred cases of primary tumor of the heart have been reported. Added refinements in the technique of radiographic investigation and electrocardiographic diagnosis and broader recognition of the fact that tumors of the heart may produce bizarre clinical pictures will lead, very likely, to the more frequent ante-mortem diagnosis of cardiac tumors than has been the case heretofore.

CASE REPORT

L. M., No. 282048, a 54-year-old stone cutter, was first admitted to the Jewish Hospital of Brooklyn on Nov. 7, 1944, complaining of edema of the lower extremities of four months' duration, exertional dyspnea, and swelling of the eyelids.

In 1936 he had melena. A gastrointestinal x-ray series at that time disclosed a prepyloric ulcer. Later that year he had a transient glycosuria of less than 1 per cent, which disappeared in a few months without insulin or special dietary precautions.

Prior to admission to the hospital, he had felt well until the gradual onset of swelling of the lower extremities, at first affecting only the ankles and then progressively involving the entire lower extremities. Associated with this there was increasing dyspnea on exertion, to such extent that even the act of dressing produced it. For two weeks prior to admission, there was puffiness of the eyelids in the morning which tended to disappear later in the day. There was also considerable enlargment of the abdomen. Just prior to admission he was put on digitalis, 0.09 Gm. per day, and ammonium chloride, 6.0 Gm. per day, which was followed by single doses of 2.0 c.c. of parenteral Mercupurin. Copious diuresis resulted without general improvement.

Physical examination on admission revealed a well-developed, well-nourished white man in no apparent distress. The blood pressure was 154/114, temperature 99° F., respirations 22, and pulse 100 per minute. The face was red. Examination of the ocular fundi showed some arteriovenous nicking. There was distention of the neck veins with a visible venous wave. Examination of the lungs revealed decreased fremitus, impaired resonance, decreased breath sounds, and fine râles at both bases and in the left axilla from the fourth rib downward. On percussion, the heart was enlarged to the left. A harsh systolic murmur was heard loudest at the apex. Also heard at the apex was a third heart sound. The liver was palpated three fingerbreadths below the costal margin and was neither tender nor pulsating. In the abdomen there was moderate shifting dullness to percussion. Pitting edema was present from the ankles to the sacral region. A reddish purple, maculopapular rash, which a dermatologist ascribed to stretching of

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Received for publication Jan. 20, 1948.

skin due to the edema, was present on both legs. This produced pruritus, scratching, secondary infection, and dermatitis. Rectal examination was negative.

Examination of the blood revealed a hemoglobin value of 97 to 104 per cent (Sahli) and a red blood cell count of 5,200,000 to 6,980,000. The sedimentation rate was 1.0 mm. in one hour and the hematocrit was 73.6 per cent of normal. Several urinalyses revealed specific gravities ranging between 1.010 and 1.022 with a trace to 2 plus albumin, no sugar, and a negative microscopic examination. The recumbent venous pressure was 280 mm. H_2O which rose to 310 mm. H_2O on right upper quadrant pressure. The arm-to-tongue circulation time (saccharine) was 65 seconds and the arm-to-lung time (ether) was 35 seconds. Blood sugar was 95 mg. per cent, urea nitrogen 20 mg. per cent, total protein 6.2 Gm. per cent with 3.57 Gm. per cent of albumin and 2.65 Gm. per cent of globulin, chlorides 346 mg. per cent, and uric acid 1.7 mg. per cent. The glucose tolerance curve was normal. Thoracic fluoroscopy showed moderate pleural effusion at the left base and good cardiac pulsations with a diffuse enlargement of the left ventricle. An electrocardiogram (Fig. 1) showed a P-R interval of 0.21 second, ventricular rate of 75 per minute, and a wide QRS complex indicative of an atypical right bundle branch block.

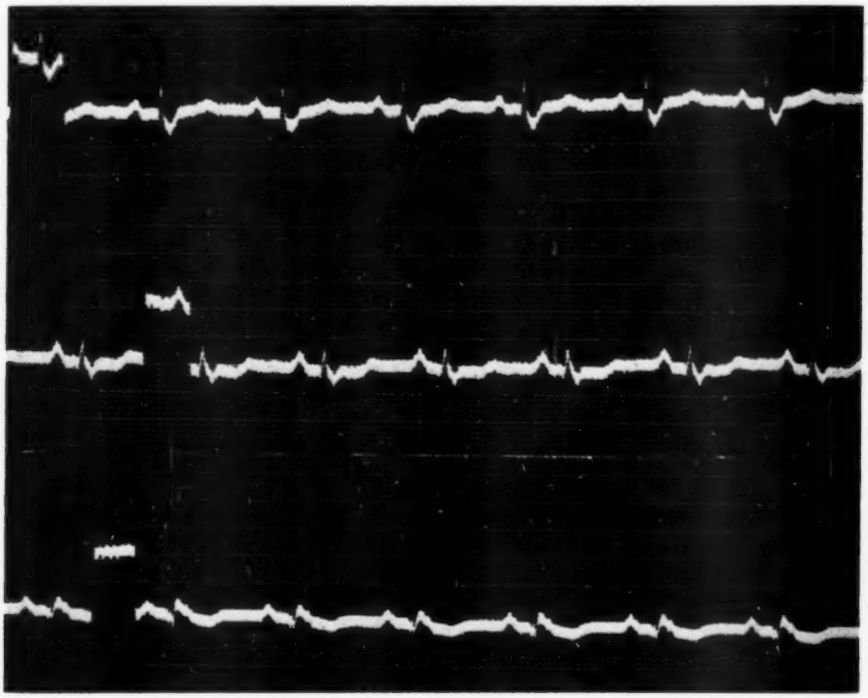

Fig. 1.—Electrocardiogram with atypical type of right bundle branch block (standard limb-leads).

The admission diagnosis was intercapillary glomerulosclerosis, but after the normal glucose tolerance curve and blood chemistry findings, this was changed to hypertensive cardiovascular heart disease with predominant right heart failure and polycythemia, probably secondary rather than primary. He was treated with digitalis and diuretics and made satisfactory clinical improvement. He was discharged on Nov. 30, 1944.

After discharge, the same program of treatment was maintained at home, but generalized anasarca recurred. In addition, he developed a purplish cyanosis of the face, neck, and extremities.

Fig. 2.

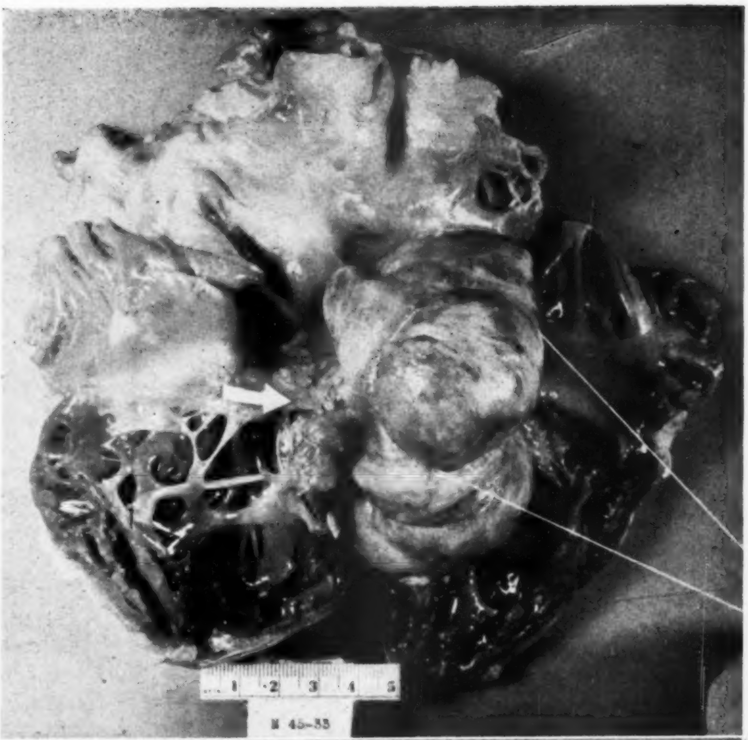

Fig. 3.

Fig. 2.—Photograph of heart with tumor retracted to show attachment to tricuspid valve.
Fig. 3.—Shows the tumor extending into the pulmonary conus.

The second and final admission to the hospital was on March 8, 1945. At that time the physical findings were comparable to those found on the previous examination, and although he presented the picture of acute myocardial failure, it was noteworthy that he could lie flat without undue distress and that he had a peculiar greenish hue overlying the mottled cyanosis of his face and upper extremities. This greenish hue was noted particularly over the skin of his knuckles and the joints of his fingers. Although there was a pronounced distention of the neck veins and a suggestion of a venous wave, it was not of the type noted in tricuspid disease. The heart was markedly enlarged both to the right and to the left. The rate was regular except for an occasional extrasystole with an average of 76 per minute. A harsh murmur occupying all of the systole was heard over the precordium, and was most intense under the sternum at the level of the fourth rib. Except for a moderate number of succulent basal râles, the pulmonary findings were negative. The abdomen was distended and a fluid wave was elicited. There was also a distinct shifting dullness. The liver was palpated readily just below the costal margin in the midclavicular line, and was neither tender nor pulsating. The cyanosis of the head, neck, and upper extremities was marked, in contrast to the slight degree of cyanosis over the rest of the body.

It was the clinical impression at that time that there was interference with the return flow in the superior vena cava. Soon after his admission late in the afternoon of March 8, 1945, the patient complained of nausea and breathlessness. He became increasingly cyanotic and restless and expired before adequate investigation could be made.

Necropsy.—The body was that of a well-developed white man weighing 82 kilograms. There was marked pitting edema of both lower extremities as high as the knees. When the abdomen was opened 4,500 c.c. of amber colored fluid was found to be present in the peritoneal cavity. The peritoneum was grayish white, smooth, and glistening. The liver edge extended to the costal margin. The pleurae were not remarkable and the pericardium was smooth and glistening. There was 10 c.c. of straw-colored fluid in the pericardial cavity.

The heart weighed 620 grams and measured 13.0 cm. from apex to base and 13.5 cm. across the base. When the right atrium was opened a large mass was seen to protrude from the region of the tricuspid valve and extend into the right atrium. The right ventricle was then opened carefully. The right atrioventricular valve measured 13.0 cm. in circumference and its contact borders were thickened. The mass referred to was attached by a broad pedicle and was continuous with the infundibular cusp of the right atrioventricular valve (Fig. 2). In this region the mass blended imperceptibly with the underlying myocardium. The external surface of the tumor was tan and gray except that at one end there was a purple discoloration. At this site the tumor was moderately soft in consistency; it was otherwise moderately firm. It assumed the shape of a solid cylinder with blunted ends and from its attachment on the tricuspid valve it passed superiorly into the right atrium and inferiorly into the right ventricle. The superior pole of the tumor reached as high as the orifices of the venae cavae and impinged upon them. Inferiorly, it passed into the right ventricle toward the apex and then upward into the pulmonary conus, extending up to the pulmonary valve but not beyond it (Fig. 3). The tumor measured 16 cm. along its outer curve, 12 cm. along its inner curve, and 4.0 cm. from one curve to the other. The cut surface of the soft, red-purple area was filled with about 5.0 c.c. of deep red, viscid material. The cut surface of the remainder of the tumor was gray-white and yellow and in most areas was coursed by narrow bands of gray-white tissue (Fig. 4). The remainder of the heart and its vessels showed nothing of note.

The right lung weighed 320 grams and the left lung weighed 240 grams. Their pleural and cut surfaces were not remarkable. The gastrointestinal tract was not unusual. The liver weighed 1,350 grams and the external surface was red-brown, smooth, and glistening. The cut surface showed a slight increase in lobular markings with a similar increase in fibrous tissue. The spleen weighed 170 grams. The cut surface showed a slight increase in fibrous markings. The bone marrow from the lower lumbar spine was cherry red in color and the consistency was softer than usual. The remainder of the autopsy was not unusual.

Microscopic Examination.—Many preparations from different portions of the tumor showed a variegated appearance (Figs. 5, 6, and 7). The tumor consisted of two main cell types. Fairly large cells which stained a deep purple and had pale vesicular nuclei were seen. These were oval, round, or spindle shaped. These hemangioblasts were arranged in nests and in an alveolar pattern. The entire tumor was highly vascular. Some areas of the tumor showed necrosis with dense infiltrations of polymorphonuclear leucocytes. In places, adjacent myocardial cells were separated from and fairly well demarcated from tumor tissue by dense bands of pink-staining fibrous tissue. The stroma was loose in some areas and the hemangioblasts therein were round and more pyknotic. The other cell component was round and palely stained. These endothelial cells were arranged in sheets between the nests of hemangioblasts; the appearance was one of a honeycomb (Fig. 6). Blood vessels were lined by both hemangioblasts and endothelial cells and the lining blended imperceptibly with the tumor tissue. Within these blood vessels both cell components were seen. Mitotic figures were nowhere seen. Preparations from the myocardium beyond the reaches of the tumor showed a slight increase in fibrous connective tissue replacing myocardial fibers.

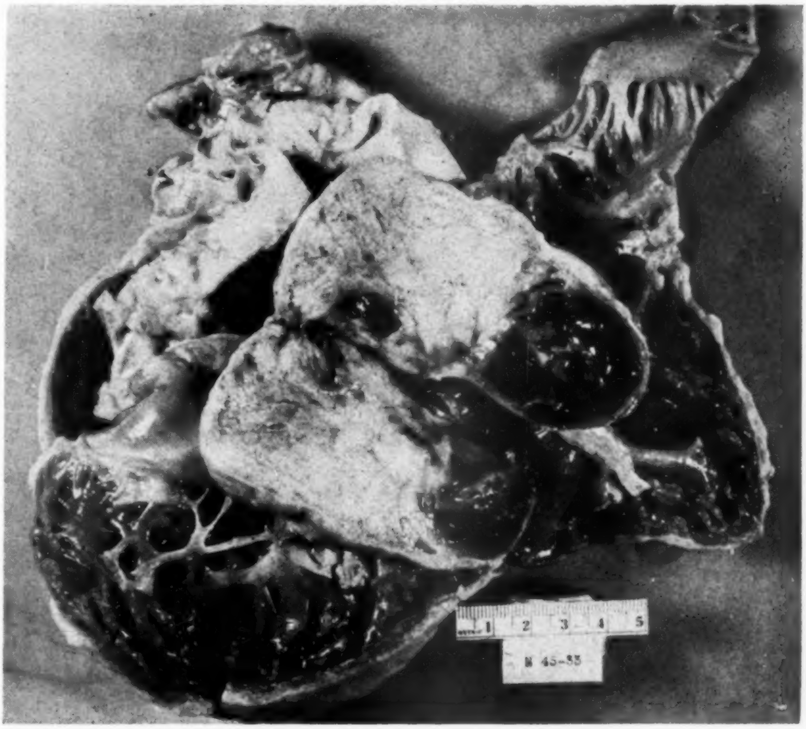

Fig. 4.—Tumor bisected to show the appearance of cut surface. Note the solid and the cystic areas filled with fluid and clotted blood

Of interest in preparations from the lung were the thick-walled blood vessels showing thrombi, some of which were recanalized. Preparations from the liver showed an increase in connective tissue which in places replaced hepatic cords. Aside from an increase in fibrous connective tissue, nothing remarkable was noted in sections from the spleen. No pathologic findings were seen in sections from the pancreas, adrenal glands, kidneys, and bone.

The final anatomic diagnosis was: Hemangio-endothelioblastoma of the right heart; congestion and cirrhosis in liver; canalized thrombi in branches of pulmonary artery; fibrosis of spleen. Myofibrosis cordis; nephrosclerosis.

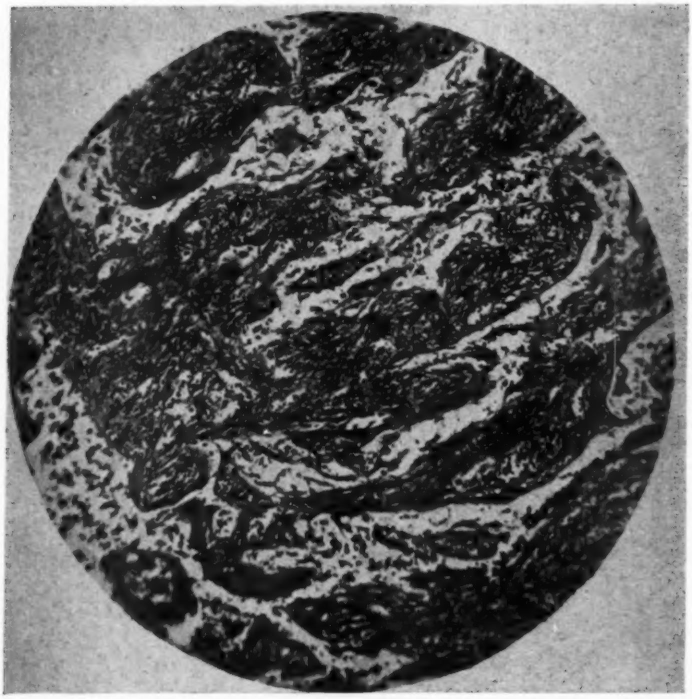

Fig. 5.—Photomicrograph to show the vascular spaces. Hematoxylin-eosin (× 120).

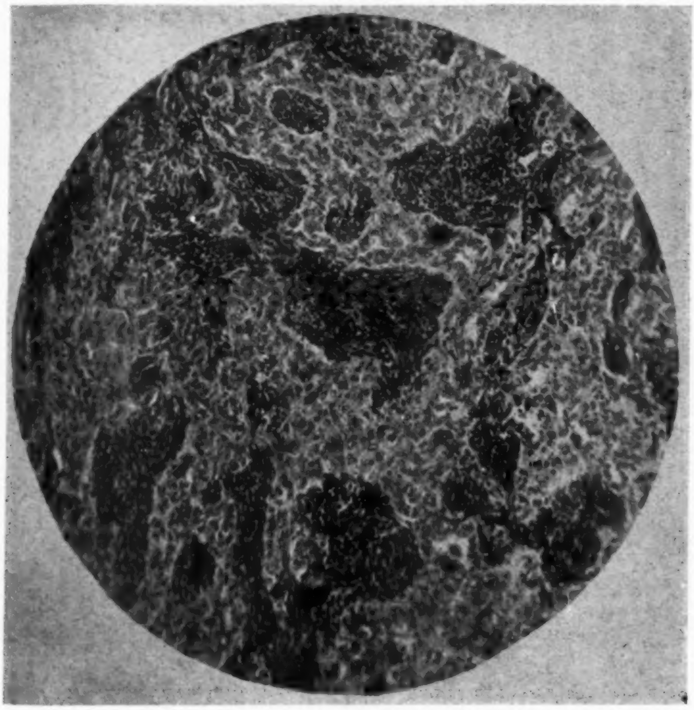

Fig. 6.—Photomicrograph of the more solid portion showing the two types of cells comprising the tumor. Hematoxylin-eosin (× 120).

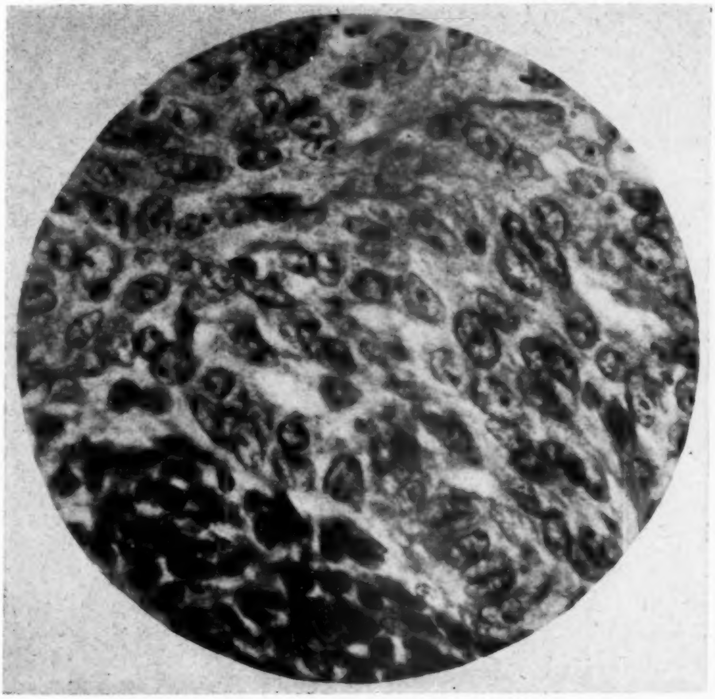

Fig. 7.—Higher power of Fig. 6 to show both hemangioblasts and the endothelial cells. Hematoxylin-eosin (× 600).

DISCUSSION

Type, Incidence, and Location of Heart Tumors.—Primary tumors of the heart which have been reported have been identified as myxoma, fibromyxoma, sarcoma, fibroma, varix, lipoma, rhabdomyoma, endothelioma, lymphangioma, lymphangio-endothelioma, hemangioma, hemangio-endothelioma, and leiomyoma.

Benign tumors comprise the greater bulk of primary tumors of the heart, and among them the myxoma is the most common. Yater[1] in his report found that 17.8 per cent of the primary tumors were malignant, while Larson and Sheppard[2] reported that 29.0 per cent were malignant. Reeves and Michael[3] have stated that the ratio of secondary to primary tumors is approximately sixteen to one. In the fifty-six cases which Lymburner[4] gathered from the Mayo Clinic from 1915 through 1931, fifty-two were secondary and four were primary. In his series, primary tumors occurred in about 0.05 per cent of the cases which came to autopsy. In a survey of our own hospital records which include approximately 5,000 autopsies extending over the period from 1922 through 1947, we have had one case of primary tumor, the present one, and eighteen cases of secondary cardiac tumors. Of the latter, fifteen were carcinoma, two were hypernephroma, and one was a lymphosarcoma. Therefore, in our series, tumors of the heart, primary and secondary, have occurred in

0.38 per cent of the cases which came to autopsy. Tumors of the heart tend to be situated in the atrium; the right atrium is a more frequent site than the left. Tumors may arise from the valves, endocardium, interventricular septum, fossa ovalis, myocardium, pericardium, and from the endothelial elements in the great vessels of the heart. Like brain tumors, heart tumors are malignant by position, regardless of their histopathology.

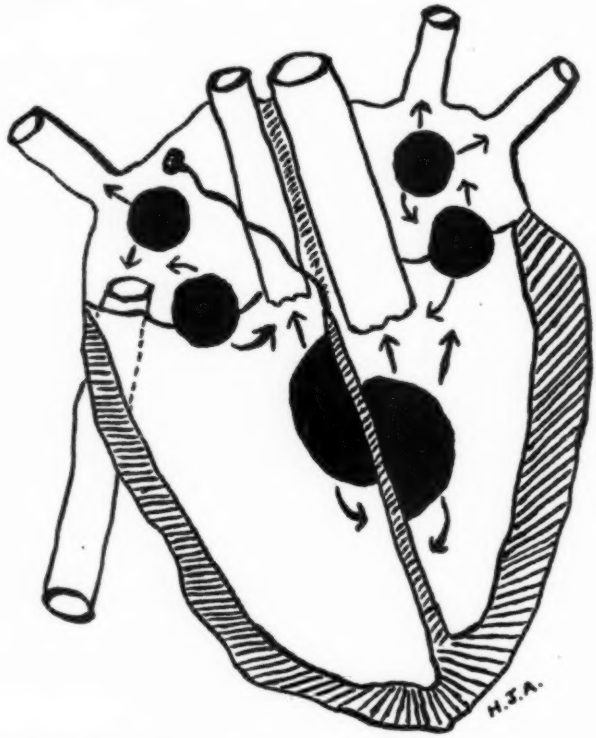

Fig. 8.—Common sites of heart tumors. Arrows indicate valvular obstruction or conduction interference that may result from growth or propagation of tumor.

Diagnosis.—Fig. 8 illustrates the common locations of cardiac tumors with arrows representing the mode of obstruction that may result. Depending upon the position and mobility of the tumor, any one of many physical signs may occur. Aortic, mitral, tricuspid, and pulmonic stenosis may occur. When tumors infiltrate or, by pressure, influence the conduction mechanism of the heart, aberrant electrocardiographic patterns occur; myocardial infiltration and pericardial effusion may also result. Because many tumors are pedunculated and attached by long stalks, ball valve obstructive phenomena are not uncommon. This is particularly frequent in cases of benign tumors. Embolic phenomena secondary to intracardiac tumors have also been reported.[5]

Tumors of the right atrium and mitral valve, with enlargement of the heart to the right on percussion, may simulate a mediastinal tumor since obstruction to the vena cava is not unusual. The venous pressure will be ex-

tremely high, as was so in our case (above 300 mm. H_2O). Sudden death occurs in patients with heart tumors and is usually the result of the mitral or tricuspid orifice being blocked. Wells and associates[6] have reported a case in which the position of the tumor was almost identical with ours.

Fairly characteristic of heart tumors is the alteration of physical signs with change in position of the patient's heart. The signs may be those of mitral insufficiency when the patient is recumbent and mitral stenosis when he is sitting. In Ravid and Sachs'[7] case the tumor was in the left atrium and extended into the pulmonary vein. This produced dyspnea when the patient was in the erect posture; there was no dyspnea when the supine position was assumed. Houck[8] reported a case in which the patient fainted upon standing. Sudden paroxysms of dyspnea and/or cyanosis occur with and without change in position and should at once arouse suspicion of a cardiac tumor. The occurrence of dyspnea which is out of proportion to the clinical findings is of utmost importance and should always suggest the possibility of intracardiac neoplasms; this symptom occurred in our case and in those others.[9,10,11]

The presence of hemopericardium is diagnostically significant. Withdrawn pericardial fluid should be mixed with 10 per cent formalin and sent to the laboratory for histologic studies. As with pleural or peritoneal fluid, the pathologist may be able to demonstrate the presence of tumor cells. There may be a rapid loss of blood and development of anemia as a result of rupture of a great vessel, usually the vena cava, as occurred in Perlstein's[12] case. The vena cava was also ruptured in the case reported by Reisinger and associates[13] and a hemopericardium was present for approximately twenty-five days.

In patients with a known primary neoplasm outside the heart the development of cardiac changes, such as arrhythmias, should suggest the possibility, or, indeed, the probability, of metastasis to the heart. Such was the course in the case reported by Barnes and associates.[14] Tumors of the atria may produce high and plateau-type P waves with or without a prolonged P-R interval. The electrocardiographic changes in the presence of tumors of the heart have been reviewed by Siegal and Young.[15]

In retrospect, when diagnoses are made more easily, our case presented several clinical features suggestive of a cardiac tumor. The very high venous pressure, prolonged circulation time, and obstruction of the vena cava are easily explained in view of the huge tumor in the right side of the heart. It was incongruous to us that a patient with so severe a degree of right heart failure should not be uncomfortable lying flat in bed. This was understandable when we ultimately learned that the anatomic position of the tumor, with its relative immobility, did not influence the degree of venous obstruction when the position of the patient (and his heart) was altered. The electrocardiogram, while showing a prolonged P-R interval and a right bundle branch block, was at most only suggestive of the lesion found. The peculiar cyanosis of our patient suggested the possibility of a tumor. The patient of Weir and Jones[16] presented a similar cyanosis (of a lesser degree, however) of the lips and finger tips and their patient had a leiomyosarcoma of the right atrium.

The use of roentgen rays as a therapeutic measure in tumors of the heart is receiving more prominence.[17] Shelburn and Aronson[18] have reported a case in which a skull or dural tumor metastasised to the heart and produced an effusion and a conduction disturbance. After x-ray therapy was directed to the heart, both the effusion and the arrhythmia disappeared rapidly.

In general, the sudden onset of signs of cardiac decompensation, particularly in a young person without pre-existing rheumatic or other heart disease should invite consideration of the presence of a cardiac tumor. Cardiac signs which are particularly suggestive are: symptoms of congestive failure which do not improve on digitalis therapy, the presence of unexplained hemopericardium, the development of an arrhythmia or heart block, localized enlargement or irregularity in the outline of the heart, and alteration of cardiac signs on change of position.

SUMMARY

A case of hemangio-endothelioblastoma of the heart is presented. The clinicopathologic features of cardiac tumors are discussed.

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ERRATUM

In the article, "Bacterial Endocarditis," by Richard C. Cecil (December, 1948), the stethogram, Fig. 1, page 935, was printed upside down.

Abstracts and Reviews

Selected Abstracts

Massell, B. F., Zeller, J. Wallace, Dow, James W., and Harting, Donald: Streptomycin Treatment of Bacterial Endocarditis. New England J. Med. **238:**464 (April 1), 1948.

Streptomycin was an effective agent in the treatment of a case of endocarditis caused by a gram-negative organism belonging to the genus *Hemophilus*. The organism was resistant to penicillin in vitro, but was inhibited by less than four units of streptomycin per cubic centimeter. Clinical improvement promptly followed the administration of streptomycin, 2.0 Gm. daily, in eight divided doses. Treatment was discontinued after 13.5 Gm. was given in six and one-half days because of the development of toxic symptoms. During treatment, the serum streptomycin level ranged from 10 to 66 units per cubic centimeter. This short, intensive course eradicated the infection.

KAY.

Fisch, C.: Complete Heart Block. New England J. Med. **238:**589 (April), 1948.

Two cases of complete heart block in young adults are presented. In each a slow heart rate had been present for several years. Neither was known to have had diphtheria or rheumatic fever. Neither had symptoms clearly referable to the heart, although each had fainted occasionally in the past. Both had systolic murmurs; one had slight cardiac enlargement, and one had T-wave abnormalities which increased in degree from 1943 to 1947. The resting pulse rates were 40 and 50 per minute, increasing with exertion to 52 and 80, respectively.

The significant clinical aspects of the disorder are discussed. The prognostic importance and difficulty of differentiating the acquired from the congenital form of complete heart block are considered.

KAY.

Fleischner, F. G., Romano, F. J., and Luisada, A. A.: Studies of Fluorocardiography in Normal Subjects. Proc. Soc. Exper. Biol. & Med. **67:**535 (April), 1948.

A study of fifteen normal subjects by fluorocardiography yielded the following observations:

(a) The tracing of the ascending aorta presents a typical pattern which is due partly to transmission of intraventricular pressure and partly to motion of the aortic root which occurs with ventricular systole and diastole.

(b) It is possible to record in certain cases a tracing of the pulmonary veins. Its most typical feature is a positive wave during presystole.

(c) The velocity of the pulse wave in the lesser circulation is much lower than in the greater circulation. It is more rapid in the smaller branches than in the stems of the pulmonary artery. Average figures are given.

(d) The tracing of the pulmonary parenchyma is the equivalent of a plethysmogram. While the rise and the ascending limb of the wave are of pulmonary arterial origin, the peak and the descending limb of the wave are probably of pulmonary venous origin.

AUTHORS.

Montgomery, G. E., Jr., Geraci, J. E., Parker, R. L., and Wood, E. H.: The Arterial Oxygen Saturation in Cyanotic Types of Congenital Heart Disease. Proc. Staff Meet., Mayo Clin. **23:**169 (April 14), 1948.

Continuous observation of the arterial oxygen saturation in man was made by the oximeter, which permits readings continuously on the intact human ear. Nineteen normal subjects and

twenty-five patients with a cyanotic type of congenital cardiac defect were studied by this means. Coincidental radial or femoral arterial blood samples were collected for analysis of oxygen content and capacity by modified Van Slyke manometric methods. Estimations were made with the subjects lying and standing and following exercise and after 100 per cent oxygen inhalation.

When the normal subjects breathed pure oxygen, their arterial saturation with oxygen increased an average of 2.7 per cent to reach 100 per cent saturation in 1.3 minutes. Under similar conditions, the cyanotic patients required an average of 3.2 minutes to elicit an increase of 6.2 percentage units in oximeter saturation readings.

The most striking differences in the responses of the arterial oxygen saturation were seen following change of position or following exercise. Normal subjects showed practically no variation. The cyanotic patients showed an average decrease in oximeter saturation reading of 2.2 percentage points when they stood up and 11.2 percentage points when they exercised on a treadmill for an average of 4.1 minutes.

In eight of the cyanotic patients, the average decrease of saturation produced by exercise, as determined by Van Slyke analysis, was 19.5 percentage points, while the simultaneous oximeter readings indicated a decrease of 13.3 points. Despite such discrepancies, the authors consider the oximeter an instrument of considerable value in estimating the degree of disability of a patient and in judging the efficacy of corrective surgical procedures in such patients.

ARKLESS.

Rabson, S. M., and Thill, L. J.: Epithelium-like Inclusions in the Heart. Am. J. Path. **24**:655 (May), 1948.

The authors report the accidental discovery at necropsy of "epithelium-like inclusions" in the heart. The patient was a 29-year-old woman, hospitalized because of chest pain, dyspnea, cough, and weakness. These symptoms had frequently recurred for more than six years. During that time she bore three children, the last one six weeks before her death.

Necropsy revealed evidence of congestive heart failure with fluid in the serous cavities. The heart was enlarged, and evidence of rheumatic disease included mitral valvulitis, bilateral atrial endocarditis, and pulmonary arteritis. Aside from these stigmata in the angle between the left atrium and the left ventricle posteriorly, peculiar solid and hollow or cystlike structures were seen with the naked eye in microscopic sections. They were chiefly subepicardial and extended for a short distance upward into the atrial myocardium and downward into the ventricle. Microscopic examination showed numerous epithelial-like structures, some solid, others dilated to form comparatively large cysts or glandlike structures filled with cellular hyaline debris. The solid cellular aggregations had an appearance suggestive of sebaceous gland epithelium. Squamous characteristics were absent. The entire collection of these "epithelial inclusions" was surrounded by a dense collagenous stroma. The authors comment on the difficulty of determining the origin of these inclusions. They believe an epicardial origin is most probable.

Similar lesions have been previously reported and generally explained on the propinquity of the heart in fetal life to epithelium-producing tissues. No opinion was offered as to the possible connection between this unusual finding and the unusual clinicopathologic findings.

GOULEY.

Newman, A. A., and Stewart, H. J.: Experience With the Schemm Regimen in the Treatment of Congestive Heart Failure. Ann. Int. Med. **28**:916 (May), 1948.

Before and after the institution of the Schemm regimen, measurements of fluid intake, urine output, and body weight were made in nine hospitalized patients who manifested varying degree of congestive heart failure. The supplemental use of mercurial diuretics was avoided unless the clinical condition of the patient made their administration imperative. During the control period, the patients were given a diet containing 2.0 to 3.0 Gm. of salt and fluids to about 1,200 c.c. in twenty-four hours, and they were confined to strict bed rest. During the Schemm regimen the same routine was followed except that fluid intake averaged from 3,000 to 5,000 c.c. daily. This regimen was maintained from four to twenty-six days; in most of the patients it was continued for one week.

Under this program, there was not a single instance of definite clinical improvement of symptoms or of disappearance of edema. Oral fluid intake in excess of 3,000 c.c. was taken with difficulty, often interfering with a full consumption of the diet. In every instance, the average daily urine output during the period in which the patient was taking large amounts of water failed to approach the amount of the daily fluid intake. In several of the patients who gained weight on the high fluid intake, the urine output was considerably below the intake of fluid. In no instance was there evidence that diuresis occurred.

Because of these observations, it is the opinion of the authors that the accepted program in the treatment of patients suffering from congestive heart failure, that is, the use of low-salt diet, restriction of fluid intake to around 1,200 c.c. daily, and the use of digitalis, mercupurin, and ammonium chloride does not require any alteration. Furthermore, they are of the opinion that the indiscriminate use of the high-fluid regimen of Schemm may be harmful in the treatment of heart failure. WENDKOS.

Saphir, O., and Amromin, G. D.: Myocarditis in Instances of Pneumonia. Ann. Int. Med. **28**:963 (May), 1948.

The purpose of this report is to correlate the clinical and post-mortem findings, in so far as the heart is concerned, in sixty-seven patients who died following an attack of pneumonia which involved at least the total of one lobe. In twenty-six of this number (38.8 per cent), histologic alterations indicative of myocarditis could be recognized. In fifteen additional cases, degenerative changes, characterized by cloudy swelling and fatty degeneration of the myocardial fibers, were present. Of the group with myocarditis, edema of the lower extremities was present in seven instances. An excess of fluid in serous cavities, except in the pleural cavities, was found in nine instances; in four of these nine, there was also edema of the lower extremities. There was no relationship between the severity and extent of the pneumonia and the degree of myocardial changes. Many of the patients who showed either no myocardial change or only parenchymatous degeneration had moderate to severe old, organizing, as well as acute, bronchopneumonia. Myocardial involvement in patients with pneumonia occurred relatively early in the course of the disease, or occurred in those instances where there was a recent spread of the disease. Exactly one-half of the patients died suddenly. In retrospect, the myocarditis was considered to be both a complication of the disease and the cause of unexpected death in thirteen patients. In fourteen of the patients with acute myocarditis, the possibility that sulpha medication was responsible for the myocardial lesions could not be entirely dismissed. WENDKOS.

Alleman, R. J., and Stollerman, G. H.: The Course of Beriberi Heart Disease in American Prisoners-of-War in Japan. Ann. Int. Med. **28**:949 (May), 1948.

Two cases of beriberi cardiovascular disease occurring in American prisoners-of-war in Japan are presented and discussed to show their contrasting clinical course and the possible factors contributing to the variability of the clinical picture.

The first case is that of a 28-year-old white man, who developed severe heart failure. When he was admitted to a hospital, teleroentgenogram of the chest revealed cardiac enlargement and passive congestion of the lungs, the electrocardiogram was abnormal by reason of low voltage and T-wave inversion in limb and precordial leads, and the blood proteins were only slightly lowered. He was immediately treated with thiamin chloride and large parenteral doses of B-complex. In view of the severity of his heart failure, it was considered advisable to use all other available measures and he was, therefore, also given Salyrgan, oxygen, and digitalis and kept on strict bed rest and a salt-free diet. The response to treatment was dramatic with an immediate diuresis and relief of symptoms and within three weeks the patient was ambulatory and asymptomatic. A repeated teleroentgenogram taken twenty days after treatment revealed a reduction in heart size to within normal limits. Five months later he was discharged from the hospital when all signs of decompensation had disappeared. However, one month following discharge he again developed profound heart failure and was rehospitalized. Evidence of cardiac dilatation was noted in the teleoroentgenogram. The electrocardiographic changes previously observed were still present. With appropriate treatment he gradually improved, but one year

later he continued to show a prolonged tachycardia on mild exertion, moderate generalized cardiac enlargement, and an unchanged abnormal electrocardiogram. One month later he again developed severe heart failure and died several days afterward, in spite of the administration of vitamin concentrates, digitalis, and diuretics. Post-mortem examination revealed marked chronic passive congestion of all the viscera. The heart was greatly enlarged and weighed 470 grams. There was considerable hypertrophy with marked dilatation of the entire heart. The consistency of the heart muscle was very flabby, with marked loss of resiliency. The valves and endocardium were normal, as were the coronary arteries. Microscopic sections showed extensive cloudy swelling, loss of striation, fragmentation, and fatty degeneration of the myocardial fibers with replacement fibrosis. There were marked interstitial edema and nuclear degenerative changes evident, with small lymphocyte and leucocyte infiltrations present. The blood vessels were dilated and were filled with red cells. The changes were considered to be consistent with those of chronic beriberi heart disease.

The second case is that of a 22-year-old white man who for forty-two months as a Japanese prisoner-of-war was also forced to subsist on similar meager rations. He, too, developed marked swelling of the legs, oral lesions, dyspnea on exertion, orthopnea, and pounding of the heart while interned in the prison camp. However, because of an ununited fracture of the leg, suffered while he was in the prison camp, he was forced to remain in the hospital for a prolonged period after his evacuation to the United States. His diet was, therefore, carefully managed and he was given large doses of vitamins for a long period of time. Under this regime, his edema, dyspnea, and heart consciousness completely disappeared within a few months. Following this clinical recovery, x-ray examinations of the chest and an electrocardiogram were made. These studies revealed no abnormalities.

Included in this paper is a very adequate review of the literature relating to beriberi heart disease. WENDKOS.

Herrmann, G. R., and Hejtmancic, M. R.: A Clinical and Electrocardiographic Study of Paroxysmal Ventricular Tachycardia and Its Management. Ann. Int. Med. **28:**989 (May), 1948.

The purpose of this report is to review the clinical features of twenty authentic cases of paroxysmal ventricular tachycardia observed by the authors during the past eighteen years and to analyze the relative effectiveness of various remedies employed by them in the treatment of this disorder. Acute myocardial infarction or digitalis toxicity was present in fifteen of the patients and fourteen had underlying chronic coronary artery disease. Two cases were relatively benign and occurred in patients with apparently normal hearts. Of the two patients with apparently normal hearts, one complained of precordial burning and one had no complaints referable to the disorder. The rates of the tachycardia varied between 110 and 220, with an average of 170 per minute. The rates were below 150 in three patients and above 200 in two. No correlation was observed between rate and prognosis, except that a continuous electrocardiogram taken during the death of the patient with the slowest rate, 110 per minute, showed a slower and slower ventricular rhythm with periods of ventricular fibrillation ending in asystole. The duration of the paroxysms varied from two hours to six days. In three of the four patients receiving no specific therapy, the disorder persisted until death.

Ten patients reverted to normal rhythm on quinidine given orally; the amount required varied from 0.6 Gm. to 5.2 Gm. in twenty-four hours. The average given in the ten cases in the twenty-four hour period before reversion was 1.5 Gm., only four requiring over 2.5 grams. In one patient with acute myocardial infarction, the rhythm was not abolished with 11.8 Gm. of quinidine given orally over a period of four days, and the patient died. Two patients in critical condition following myocardial infarction were given quinidine intravenously. One had not responded to intravenous dosages of morphine of 11, 11, and 32 mg. and oral quinidine totaling 2, 5, and 3.3 Gm. on three successive days. This patient reverted to normal rhythm after 1.7 Gm. of quinidine sulfate was given by slow intravenous drip. Another patient, who was admitted in shock, showed no change in rhythm after being given 0.6 Gm. of quinidine sulfate intravenously in 10 c.c. of distilled water, and died in one hour. One patient under treatment for

subacute bacterial endocarditis was given 1.0 Gm. of quinidine sulfate intravenously in divided doses over a period of twelve hours, and then reverted to normal rhythm after the intravenous administration of 1.2 mg. of Cedilanid. The intravenous administration of 16 mg. of morphine sulfate resulted in immediate cessation of the abnormal rhythm in one patient with myocardial infarction. In another patient the ventricular tachycardia reverted to sinus rhythm on carotid sinus pressure six minutes after 45 mg. of morphine sulfate had been given intravenously; previously the tachycardia had been unaffected by repeated carotid sinus stimulation and 32 mg. of morphine sulfate. WENDKOS.

Raab, W.: Adreno-Sympathogenic Heart Disease (Neurohormonal Factors in Pathogenesis and Treatment). Ann. Int. Med. **28**:1010 (May), 1948.

In the opinion of the author, electrocardiographic and/or clinical features of angina pectoris sudden cardiac death without significant morphologic pathology, thyrotoxic heart disease, beriberi heart disease, hypertensive heart disease, coronary sclerosis, and the cardiac component of the syndrome produced by hyperfunctioning adrenal tumors are to be related to metabolic changes within the myocardium resulting from the local accumulation of the products of excessive adrenosympathetic discharges. For this reason, the best approach in the treatment of these conditions is to prevent or suppress excessive adrenosympathetic activity and/or to desensitize the heart to the pathogenic effects of epinephrine-sympathin through correction of a sensitizing hormonal situation or through administration of adrenosympatholytic drugs. The first objective can be effectively accomplished by the following methods: (a) surgical removal of pheochromocytomas or of paragangliomas or excision of the epinephrine-sympathin producing and discharging nervous apparatus of the heart by means of ganglionectomy, sympathectomy, and pericoronary neurectomy; (b) the use of sedatives and the recommendation of physical and emotional rest in order to minimize the central stimuli for adrenosympathetic neurosecretory activity; (c) roentgen irradiation of the adrenal glands; and (d) roentgen irradiation of the thoracic sympathetic nerves. The second objective can be effectively accomplished by the use of thiouracil, surgical removal of the thyroid gland, the administration of testosterone propionate, and the administration of sympatheticolytic drugs such as dibenamine hydrochloride and ergot alkaloids, and the administration of a low-sodium and fat-free diet. In the opinion of this author, the effectiveness of nitroglycerin during attacks of angina pectoris is to be attributed to the action of this drug in counteracting the influences of epinephrine-sympathin directly within the heart muscle rather than to a dilatation of coronary vessels. WENDKOS.

Kaufman, R. E.: Immediate Fatalities After Intravenous Mercurial Diuretics. Ann. Int. Med. **28**:1040 (May), 1948.

A 21-year-old white woman was admitted to the hospital with marked edema of the legs, thighs, abdominal wall, face, and eyelids. The blood pressure was 108/70. The rest of the physical examination was entirely negative. Laboratory examinations revealed the typical findings of lipoid nephrosis. During a three-week period, she received seven injections of a mercurial diuretic intravenously. No untoward reactions followed any of these injections. Four weeks after the seventh injection, another intravenous injection of mercupurin was administered. A total of 2.0 c.c. was given within a period of about one to one and one-fourth minutes after having drawn back about 0.4 c.c. of blood. Within thirty to forty-five seconds after the end of this injection, the patient suddenly became pale, looked startled, was not able to talk, and gasped a few times. The eyes rolled and the pupils dilated wildly, the arms and legs jerked convulsively, and there was incontinence of feces. Soon respirations ceased and the pulse could not be obtained. It was presumed that death resulted from the direct action of the mercury on the cardiac musculature, causing changes in intraventricular conduction and terminal ventricular fibrillation. The author also summarizes briefly the data in thirty-one previous reports of sudden death due to intravenous injections of mercurial diuretics. Suggestions for the prevention of fatal reactions from mercurial diuretics are also included. WENDKOS.

Potts, W. J., and Gibson, S.: Aortic Pulmonary Anastomosis in Congenital Pulmonary Stenosis. J. A. M. A. **137**:343 (May 22), 1948.

The authors operated on a series of fifty-two children with congenital pulmonary stenosis. In forty-five of the patients a direct anastomosis between the aorta and a pulmonary artery was performed. In seven patients the operation proved to be exploratory only; one patient was an unrecognized case of the Eisenmenger complex not remediable by surgery, and the remaining six patients were hopeless from the surgical point of view because operation revealed the pulmonary arteries to be strandlike and bloodless (pulmonary atresia).

Of the fifty-two patients submitted to operation, the preoperative diagnosis in forty-eight was the tetrology of Fallot. The characteristic clinical findings in these patients are described. Absence of a murmur, the presence of a large pulmonary conus, or the presence of gross cardiac enlargement militates against the diagnosis of tetrology of Fallot. In none of the authors' cases was the heart size enlarged more than 25 per cent. In seven of this series of cases of the tetrology, a right aortic arch was present; in these instances the surgical approach was through the right side of the chest, and anastomosis was performed to the right pulmonary artery. In the remaining cases the aorta was anastomosed to the left pulmonary artery through a left chest approach.

The preoperative clinical diagnosis in four of the fifty-two operative cases was tricuspid atresia. The clinical picture is identical with that of the tetrology of Fallot except for two distinguishing features: a left axis deviation is present in the electrocardiogram and there is an absence of the normal fullness of the region of the right ventricle roentgenographically.

Four deaths occurred in the group of forty-five cases in which aortic-pulmonary anastomosis was performed, a mortality of 8.8 per cent. Cerebral thrombosis caused the death of two children, both of whom had suffered cerebral accidents in the past; tension pneumothorax and hemorrhage into the hypothalamus were responsible for death in the other two cases.

Of the forty-one patients who survived surgery, thirty-nine were greatly improved and showed absence of cyanosis, gain in weight, and marked increase in exercise tolerance; the other two patients were only partially relieved of their cyanosis. The longest follow-up in the series was one year. In all patients followed after surgery the persistence of a soft systolic and diastolic humming murmur indicated patency of the anastomotic opening. Postoperatively there was a fall in the erythrocyte count and hematocrit reading and an average increase of 30 per cent in the arterial oxygen saturation level. Clubbing of the fingers and toes disappeared within four to six months. In every patient followed after operation, cardiac enlargement occurred, being pronounced in three children. Although no signs of heart failure developed, the authors feel that decompensation may well occur in the future.

Of the seven operative cases in which anastomosis could not be effected, three patients died as a result of the surgery. The authors point out that those patients who have pulmonary atresia and cannot consequently receive the benefit of anastomosis withstand the shock of opening of the chest poorly.

HANNO.

Pickering, G. W.: Transient Cerebral Paralysis in Hypertension and in Cerebral Embolism. J. A. M. A. **137**:423 (May 29), 1948.

Pickering divides hypertensive encephalopathy into two categories which, he feels, differ from each other both clinically and pathologically.

1. The first category embraces the encephalopathy occurring in the acute hypertension of acute nephritis, in the toxemia of pregnancy, and in cases of chronic hypertension with acute exacerbation. Clinically, there is headache, vomiting, convulsions, and coma, and evidences of transient focal brain involvement are sometimes present. The pathologic basis for this type of encephalopathic attack is cerebral edema. Although the factors giving rise to cerebral edema in these cases are not as yet fully known, Pickering believes that it is more likely that defective constriction of the cerebral arteries rather than excessive constriction is involved.

2. The second category comprises the hypertensive encephalopathy of chronic hypertension. Clinically the picture is dominated by evidences of focal brain involvement with complete or partial recovery. Pickering believes that the widely held concept of localized cerebral arterial spasm advanced to explain these episodes is untenable. He points out that the cerebral arteries

have poorly developed muscular walls and react to vasoconstrictor agents by only feeble constriction. He demonstrates by case histories that the type of clinical attack in the hypertensive encephalopathy of chronic hypertension closely resembles the disorders due to cerebral embolism seen in nonhypertensive patients with mitral stenosis and auricular fibrillation. He feels, as a result of clinical and pathologic studies, that the true pathologic basis underlying the encephalopathic attacks of chronic hypertension is organic cerebral arterial obstruction (thrombosis) with resultant focal brain damage. The recovery, complete or partial, which ensues may be explained by the development of collateral circulation. HANNO.

Beck, C. S., Stanton, E., Batiuchok, W., and Leiter, E.: Revascularization of Heart by Graft of Systemic Artery Into Coronary Sinus. J. A. M. A. **137**:436 (May 29), 1948.

Beck and his co-workers set forth the details of their preliminary animal experiments on a new surgical method for improving coronary circulation.

Previous investigators have shown that ligation of the coronary sinus in dogs resulted in dilatation of the intramyocardial collateral channels. Taking their cue from this work, Beck and his group ligated the coronary sinus in dogs, following this procedure by anastomosing the common carotid artery to the sinus or by anastomosing one end of a 5.0 cm. arterial graft to the descending aorta and the other end to the coronary sinus. The animals generally tolerated the anastomosis well. Following the completion of the operation, the coronary sinus became distended and frequently pulsations were noted; the veins became pink and the heart seemed to improve in color. None of the animals successfully operated upon developed cardiac dilatation or hypertrophy or cardiac failure, and no electrocardiographic changes were noted postoperatively.

In a series of ten dogs with functioning anastomoses, subsequent ligation of the descending branch of the left coronary artery resulted in no immediate deaths; two dogs died, respectively, eight and thirteen days later, and eight dogs recovered. Anatomic studies of the ten hearts revealed no evidences of infarction in four of the recovered group and only scattered areas of necrosis in the other six dogs (including the two which died); in no specimen of this group was there necrosis involving the entire thickness of the myocardium.

In a second series of ten dogs in which the anastomosis was completely occluded by thrombus, coronary artery ligation resulted in seven deaths and three recoveries, the deaths occurring from one to forty-eight hours after arterial ligation was effected. In fifty normal dogs, coronary artery ligation produced a 70 per cent mortality, and in fifty-seven dogs with ligation of the coronary sinus, followed some time later by ligation of the coronary artery, the mortality was 61 per cent. The hearts of the control animals showed extensive myocardial destruction.

Following ligation of the coronary sinus, two possible means of exit for the blood in the sinus exist: through the intramyocardial channels which empty into the chambers of the heart, and through a system of superficial veins which drain blood from the coronary sinus system into the right atrium. Injection studies of twenty-two hearts following the anastomosis procedure showed that in only two specimens was the superficial venous route of any particular significance. In order to eliminate the possibility of this undesired result, the authors propose to ligate the superficial veins draining blood away from the coronary sinus when the anastomosis is done on human patients.

Blood flow studies were performed by injection of heparinized blood into the coronary sinus of the hearts of normal dogs, of hearts with ligated sinuses, and of hearts of animals upon which carotid anastomosis had been effected. The retrograde flow, as measured by the amounts of blood recovered from the left coronary arteries, was augmented over the normal in those specimens with ligation of the sinus alone. The recovery of blood was of about the same order of magnitude in the hearts with patent anastomosis as in the normal hearts. The authors interpret this latter finding to be evidence against the presence of any marked fistula effect following anastomosis either in the myocardium or in the superficial venous channels draining directly into the right atrium.

Brief mention is made of the first human being with coronary disease in whom coronary sinus ligation and anastomosis between the sinus and the aorta by means of a brachial artery graft was performed. The patient tolerated the operation, and the case will be reported in detail in the future. HANNO.

Brown, G. E., Jr., Wood, E. H., and Lambert, E. H.: The Effects of Intravenous Injection of Tetra-Ethyl-Ammonium Chloride on the Intra-Arterial Blood Pressure and Other Physiological Variables in Man. J. Pharmacol. & Exper. Therap. **93:**10 (May), 1948.

Intra-arterial blood pressure, pulse rate, plethysmographic measurement of changes in leg volume, and intrarectal pressure were continuously recorded before, during, and after the administration of tetra-ethyl-ammonium chloride, intravenously, in eight human subjects. The drug was given in doses of 5.5 to 7.7 mg. per kilogram of body weight.

There was a fall in systolic blood pressure but no consistent change in diastolic pressure. The pulse rate rose; there was an increase in the volume of the leg, and a decrease in intrarectal tonus. The changes occurred within thirty-nine seconds after the start of the injection and, except for intrarectal tonus, continued for twenty to twenty-five minutes. Decreased intrarectal tonus persisted for as long as seventy-two minutes. GODFREY.

Braun, H. A., and Lusky, L. N.: A Comparative Study of the Intravenous Pigeon and the Intravenous Cat Method in the Assay of Digitalis. J. Pharmacol. & Exper. Therap. **93:**81 (May), 1948.

The authors found that digitalis preparations could be as easily assayed and standardized with pigeons as with cats. The technique of the assay is similar to that of the United States Pharmacopeia.

The primary importance of the authors' findings is that pigeons are more available and cheaper than cats. GODFREY.

Lehmann, G., and Randall, L. O.: Pharmacological Properties of Sympathomimetic Diamines. J. Pharmacol. & Exper. Therap. **93:**114 (May), 1948.

The chemical structure of epinephrine, neosynephrine, phenethylamine, ephedrine, propadrine, and benzedrine was altered so that a series of twenty-five aromatic and aliphatic alkylene α, β-diamines were studied with reference to their depressor activity, bronchodilator activity, and central stimulating activity. In general, the derivatives of these drugs proved less toxic and less potent in regard to vasopressor and bronchodilator effects.

Two compounds were synthesized which resembled ephedrine in pressor potency and duration of action but were only one-third as toxic, lacked the central nervous system stimulating effects, and did not produce tachyphylaxis. If further studies corroborate these findings, these compounds would seem to possess ideal characteristics for a pure pressor drug.

GODFREY.

Aisner, M., and Hoxie, T. B.: Bone and Joint Pain in Leukemia, Simulating Rheumatic Fever and Subacute Bacterial Endocarditis. New England J. Med. **238:**733 (May 20), 1948.

Four young patients with acute lymphatic leucemia are presented to demonstrate that this disease, at certain stages, may clinically simulate acute rheumatic fever or subacute bacterial endocarditis. The symptoms and signs common to all three illnesses include weakness, fatigability, weight loss, fever, sweats, bone and joint pain, muscle pain, painful fingertips, abdominal pain, anorexia, vomiting, epistaxis, pallor, shortness of breath, palpitation, anemia, hemorrhagic skin lesions, inflamed joints, lymphadenopathy, splenomegaly, tachycardia, and heart murmurs.

The hemoglobin, red cells, and platelets may remain nearly normal for several weeks after the development of symptoms of leucemia, and the later changes may parallel those in rheumatic fever and subacute bacterial endocarditis. The total white blood cell counts in the four patients were 3,800, 5,500, 13,400, and 278,000; hence, in three of the four, the correct diagnosis would not have been suspected from this study. A careful differential white cell count is of great value in the differential diagnosis. A high percentage of lymphocytes, especially when associated with leucopenia, is presumptive evidence against rheumatic fever. The diagnosis of leucemia is readily established when young forms are present in abundance.

The joint symptoms and signs in leucemia may be indistinguishable from those of acute rheumatic fever. The x-ray appearance of the bones is occasionally helpful. KAY.

Luisada, A. A., and Fleischner, F. G.: Dynamics of the Left Auricle in Mitral Valve Lesions. Am. J. Med. 4:791 (June), 1948.

Fluorocardiographic tracings of the left auricle were recorded in twenty-three patients with lesions of the mitral valve. The patients were about equally divided into two groups: one with sinus rhythm and the other with auricular fibrillation.

A typical pattern was found in nine of ten patients with fibrillation and in ten of thirteen patients with normal sinus rhythm. This consists of a positive plateau which is evidence of expansion of the left auricle during ventricular systole because of regurgitation. A description of the distinctive features of this pattern is given. Another variation, consisting of abnormalities in shape and depth of the presystolic auricular wave, is found in certain patients with sinus rhythm and is explained as the result either of severe narrowing of the mitral valve or of a structural lesion of the left auricular wall. The practical diagnostic value of these graphic signs is discussed.

The existence of a pure mitral stenosis, not accompanied by mitral insufficiency, was not demonstrated in the present study. AUTHORS.

Master, A. M.: Digitoxin Intoxication. J. A. M. A. 137:531 (June 5), 1948.

Digitoxin has become one of the most widely used digitalis preparations. Gold found that 1.2 mg. of digitoxin, given initially for single-dose digitalization and followed by 0.2 mg. daily for maintenance, provided a satisfactory dosage schedule for 75 per cent of his series of cases. Master points out that of all the digitalis glycosides, digitoxin has the greatest cumulative action and that the recommended dosage cannot be used indiscriminately for all patients. He presents a group of nine cases of digitoxin intoxication which illustrate the hazard of disregarding the patient's weight and individual tolerance and response to the drug. Master stresses the necessity for individualization in the use of digitoxin and states that the daily maintenance dose may vary from 0.05 mg. to 0.2 milligram. HANNO.

Chapman, E. M., Kinsey, D., Chapman, W. P., and Smithwick, R. H.: Sympathetic Innervation of the Heart in Man: Preliminary Observations of the Effect of Thoracic Sympathectomy on Heart Rate. J. A. M. A. 137:579 (June 12), 1948.

Studies in man and in dogs have demonstrated that cardioaccelerator fibers are derived from both the left and right second, third, fourth, and fifth thoracic sympathetic ganglia, and it has been observed that the pulse rates of totally sympathectomized dogs even after exercise are markedly slower than in normal dogs.

The authors studied a group of nineteen patients who, for various reasons, had undergone thoracic sympathectomy. The sympathectomies included the second to the fifth thoracic ganglia in all but two patients; in these, surgery had been limited to the second and third dorsal ganglia. Bilateral sympathectomy had been performed on sixteen of the nineteen patients. A reduction in the resting pulse rate and a diminished heart rate response to exercise were observed almost uniformly. The effect was more noticeable after both sides had been operated upon than after unilateral thoracic ganglionectomy. It was noted that the effect on the pulse rate in patients who had had extensive resections of the sympathetic ganglia was no greater than in those in whom only the second to the fifth thoracic ganglia, inclusive, had been removed bilaterally.

HANNO.

Fishberg, A. M.: Sympathectomy for Essential Hypertension. J. A. M. A. 137:670 (June 19), 1948.

An analysis of the results of sympathectomy in a series of 119 cases of essential hypertension is presented. The Smithwick thoracolumbar sympathectomy was performed on 109, the Peet supradiaphragmatic procedure on eight, and the Adson infradiaphragmatic operation on two patients.

There was no consistent correlation between the results of the sodium amytal test and the postoperative blood pressure changes, and the test proved of little value in the selection of patients for sympathectomy.

Following sympathectomy there was a fall in blood pressure to levels near normal in most patients for a period of several weeks or months. Then, as a rule, the pressure gradually rose. After the postoperative stabilization in blood pressure, it was found that the diastolic pressure was 25 per cent or more below the preoperative level in 25 per cent of the patients and that the systolic pressure was 25 per cent or more below the preoperative level in 32 per cent of the patients. There was an average fall in systolic blood pressure of 16 per cent and in diastolic pressure of 13 per cent.

Worth-while symptomatic improvement followed sympathectomy in fifty-nine of the 100 patients who had symptoms due to hypertension preoperatively. Headache was the symptom which was especially relieved, disappearing entirely or almost completely in sixty-four of the eighty-three patients who had suffered from severe headache before surgery. There was no recurrence of the episodes of hypertensive encephalopathy in the four patients who had previously experienced them. In several instances gallop rhythm disappeared, the inverted T waves of left heart strain became upright, and decrease in the size of the enlarged heart occurred. Of the seventeen patients with papilledema, accompanied in fifteen by hemorrhages and exudates, twelve showed clearing of the retinal abnormalities following surgery. In three of these patients retinopathy recurred, but in four the disc and retina were normal in follow-up observations of forty-five to seventy-one months. Headache was relieved and retinal abnormalities disappeared in many patients who showed no decrease in blood pressure following surgery, but in no instance was an increase in the caliber of narrowed retinal arteries observed. The relief of headache and the improved fundoscopic picture postoperatively is ascribed to a redistribution of the blood so that a smaller fraction of the cardiac output is distributed to the cephalic portion of the body with resultant decrease in blood flow to the head.

It cannot be categorically stated whether life is prolonged by sympathectomy, but the author feels that the outlook for life is probably improved by surgery, as opposed to conservative medical management, in those patients with retinopathy who show disappearance of the retinal lesions postoperatively and in those who exhibit marked lowering of blood pressure with decrease in the amount of cardiac enlargement and disappearance of the electrocardiographic pattern of left heart strain following surgery.

A number of untoward effects of sympathectomy were noted. The operative mortality was 3.5 per cent. Following lumbar ganglionectomy, absence of ejaculation often resulted. Arteriosclerotic symptoms (intermittent claudication, angina pectoris, myocardial infarction, and mental changes) were sometimes precipitated, evidently as a result of a lower pressure head and consequent decreased blood flow through already sclerosed vessels. In addition, the period of hospitalization of over a month, the frequent occurrence of postural hypotension postoperatively, and the economic burden are further disadvantages. In none of the patients operated upon could it be stated that a cure had been effected.

From an analysis of the desirable and undesirable results following sympathectomy in his series of 119 cases, Fishberg concludes that sympathectomy is a palliative measure only and is indicated in less than 4 per cent of patients with essential hypertension. HANNO.

Roberts, A. M., and Askey, J. M.: Temporal Arteritis: Relief of Headache by Injection of Procaine Hydrochloride. J. A. M. A. 137:697 (June 19), 1948.

Periarterial injection of procaine hydrochloride (1.0 to 2.0 c.c.) produced marked and lasting relief of pain in four cases of cranial arteritis involving chiefly the temporal arteries. From one to six injections were necessary. In one case it was felt that intracerebral arteries were involved, and block of the stellate ganglion was performed with satisfactory results. Concomitant with the immediate relief of pain afforded by periarterial procaine injection, the hard, tortuous, involved vessels became soft and relaxed. This finding and the fact that one of the patients was only 25 years of age suggest that cranial arteritis is of vasospastic nature. The arteritis in all four patients followed in the wake of an acute infection; this is taken as evidence of an infectious basis of this disorder.

The authors point out that the injection treatment is simpler and more practicable than arteriectomy because there is often multiple involvement of cranial arteries.

HANNO.

Garland, L. H., and Thomas, S. F.: Roentgen Diagnosis of Myocardial Infarction. J. A. M. A. **137**:762 (June 26), 1948.

A series of 249 patients with various cardiac disorders was studied electrocardiographically (standard limb leads and Lead IVF) and by multiple-slit roentgen kymography. In each case comparison was made of the presence or absence of electrocardiographic evidences of myocardial disease with the presence or absence of kymographic evidences of myocardial disease as manifested by localized diminution or absence of pulsation, parodoxic pulsation, or pronounced diastolic irregularities. Correlation between the two methods of study occurred in 201 cases (80.5 per cent).

Of the 249 cases studied, a clinical diagnosis of myocardial infarction had been made in fifty-eight instances. In this group there was correlation between the electrocardiographic and kymographic findings in thirty-three cases (56.8 per cent). In ten cases the kymographic findings led to a correct diagnosis of infarction despite negative electrocardiographic or indefinite clinical findings.

The authors feel that roentgen kymography is a valuable aid in the diagnosis of myocardial infarction in those patients in whom the clinical picture is atypical or the electrocardiogram is inconclusive.

HANNO.

Reuling, J. B., and Cramer, C.: Subacute Bacterial Endocarditis: Report of Two Cases. J. A. M. A. **137**:785 (June 26), 1948.

The authors report two cases of subacute bacterial endocarditis due to the *Streptococcus viridans* in which cures were finally effected by penicillin after failure of previous courses of penicillin.

The first patient, a 36-year-old Negro, received an initial course of 2.6 million units of penicillin over a thirteen-day period and a second course of 2.5 million units over a similar period. Seven and four weeks, respectively, after completion of the first two courses of the drug, positive blood cultures recurred. A third course of penicillin, totalling 7.8 million units administered over a period of thirty-nine days, brought about cure. The patient has remained well with negative blood cultures during a three-year follow-up.

The second patient, a 53-year-old white man, relapsed two days after completion of an initial course of penicillin totalling 2.0 million units given over a seven-day period, but cure resulted from a second course of 22.2 million units administered over a period of forty-five days. The patient remains well after nine months.

The authors make the point that the usually recommended doses of penicillin may sterilize the blood but may not be curative. For purposes of cure, much larger doses are often required in individual patients.

HANNO.

Green, M. B., and Beckman, M.: Obesity and Hypertension. New York State J. Med. **48**:1250 (June 1), 1948.

The authors' report is based on a study of 1,260 obese patients. One hundred forty-nine (11.8 per cent) showed hypertension. Systolic and diastolic hypertension were present in ninety-seven (65 per cent), diastolic in seventeen (11.4 per cent), and systolic hypertension in fifteen (10 per cent). Twenty (13.4 per cent) had a normal pressure at the start of treatment but developed hypertension during the course of treatment or within a few years. The treatment in obese patients consisted, in addition to a dietary regimen, of the use of benzedrine and phenobarbital.

In the group of 149 hypertensive patients it was noted that with a reduction in weight, a fall of blood pressure to normal was found in about one-half of the patients with both a systolic and diastolic hypertension, as well as in 80 per cent of those with either a systolic or diastolic hypertension alone. The improvement of the hypertension was transitory, however, in more than one-half of the re-examined patients.

In the group of twenty patients with initially normal pressures, in four there was an increase of blood pressure to an abnormally high range during the first course of treatment, regardless of weight loss. In the other sixteen, the first high reading was noted after a time interval of four months to four years, the average being after one and seven-tenths years. Fifteen developed a systolic and diastolic hypertension; only five, a diastolic hypertension.

Their study indicates that only a relatively small proportion of obese patients show hypertension, and the majority are only slightly to moderately overweight. The age distribution of hypertensive, obese patients was almost identical to that in essential hypertension. There was no uniform reaction to weight reduction. After a notable weight loss, a fall of blood pressure to normal levels was seen almost as often as no change in blood pressure. Hypertension was likely to return in some of the improved patients after gain of weight.

The authors assume that hypertension in obese people is not caused by obesity. The same factors which cause hypertension in nonobese people are responsible for abnormally high pressures in the obese. Overweight only aggravates the condition. BELLET.

Dry, T. J., Harrington, S. W., and Edwards, J. D.: Irreversible Cardiac Disease in Adult Life Caused by Delayed Surgical Closure of a Patent Ductus Arteriosus: Report of a Case. Proc. Staff Meet., Mayo Clin. **23**:267 (June 9), 1948.

For the most beneficial effects and prolongation of life, surgical treatment must be instituted prior to the onset of irreversible cardiac changes due to the vascular shunt.

The case presented is that of a man, first seen at the Clinic at the age of 21 years, when he was in congestive heart failure. An enlarged heart had been noted at the age of 7 years. Exertion on dyspnea soon developed. Cardiac arrhythmia was found at 19 years and digitalization instituted. Cardiac enlargement, auricular fibrillation, and a machinery murmur and thrill were present in the left second and third intercostal spaces.

Following relief from congestive cardiac failure, a fistulous type of patent ductus arteriosus was triply ligated successfully and almost uneventfully. The murmur and thrill disappeared, but cardiac enlargement and auricular fibrillation remained. Mild congestive failure appeared only when digitalis was not taken. The patient died suddenly four and one-half years after operation.

Examination of the enlarged (775 grams) heart showed that the ductus was closed. Significantly, the endocardium of the left atrium and ventricle was thickened by the presence of collagen and elastic tissue, and the underlying myocardium showed an abundance of elastic tissue fibers. These thickenings, once formed, remain unchanged even in patients in whom there is a return of the chambers to normal size. In the left pulmonary artery at a position opposite the pulmonary mouth of the obliterated ductus, a raised corrugated intimal plaque was taken to be a "jet lesion," due to trauma induced by the forceful jet of blood, and persisting after closure of the ductus.

This case emphasizes the importance of operating upon patients with patent ductus arteriosus before complications develop. A technical factor also supports the recommendation of earlier and easier operation, namely, the shortening of the ductus with increasing age. The optimum age for operation is believed to be between 3 and 9 years. ARKLESS.

Jenkins, H. P., Senz, E., Owen, H., and Jampolin, R.: Control of Arterial Hemorrhage by Gelatin Sponge "Cuff" and Chromic Surgical Gut Sheath: A New Experimental Method. Arch. Surg. **55**:637 (Dec.), 1947.

The authors point out that, ideally, maintainence of blood flow through a large artery is accomplished following trauma by the suture method of closure of a defect in the wall of the artery. In other instances, the nonsuture Vitallium tube method may be of value. However, the authors point out that both of these methods require a certain amount of technical skill and experience, and further, that the patient's condition may not warrant the time necessary to carry them out satisfactorily. It was, therefore, their aim to develop a method which would be relatively simple to use and successful in the vast majority of occasions in which it was applied.

The experiments were carried out in dogs under general anesthesia and the lower abdominal aorta was exposed; after clamping with rubber-shod clamps, two defects were made in the wall by the passing of a scalpel through the entire thickness of the artery in a longitudinal direction.

Excellent control of the hemorrhage was effected by application of a cuff of dry, compressed gelatin sponge, which in turn was surrounded by a sheath of chromic surgical catgut. The sheath was held in place with several snug ligatures of chromic catgut. In sixteen animals thus treated, there was a blowout on the fourth day in one experiment, and on the seventeenth day in another.

The authors conclude that this method may well serve as a "secondary line of defense" against blowouts where arterial suture has been performed for a wound in the vessel, and especially where it has been impossible to carry out a careful suture.

LORD.

Eaton, R. M.: Pulmonary Edema, Experimental Observations on Dogs Following Acute Peripheral Blood Loss. J. Thoracic Surg. **16**:668 (Dec.), 1947.

In an extensive experimental study, Eaton demonstrated in dogs that acute hemorrhage of 25 per cent of blood volume from the femoral artery resulted in the following circulatory changes: relative anoxia, increase in capillary permeability, fall in the systemic arterial and venous pressures; a decrease in cardiac output; and early increase in pressure in the pulmonary artery, which was due to an increase in the transudation of fluid into the alveoli. The author demonstrated marked increase in pulmonary moisture and increase in pulmonary lymph flow, a fall in the plasma protein level, and elevation in the hematocrit reading. Many of these changes were temporary, and within a few hours returned to normal. However, pulmonary edema continued for several days and was readily demonstrable microscopically, in spite of the fact that the animals showed normal behavior.

In his discussion, Eaton points out that from a practical point of view acute hemorrhage which occurs at operation and is not balanced immediately by transfusion can be responsible in a matter of a few minutes for the changes in the pulmonary circulation just described. Further, pulmonary edema, which is a stagnant alveolar accumulation of high protein value, is an excellent culture media for droplet implantations from the nose and throat and, hence, for the subsequent development of pneumonia.

The author studied the use of infusions of saline, plasma, and blood in an attempt to see whether these fluids, given intravenously, would alter the changes found in the lungs. He demonstrated that intravenous saline markedly aggravated the pulmonary edema, whereas blood and plasma had only slight deleterious effects.

LORD.

Loeffler, W., and Maier, C.: Case of Felty's Syndrome With Cyclic Agranulocytosis. Cardiologia **12**:195, 1947-1948.

A 24-year-old farmer, following an atypical pneumonia with pleural effusion, developed splenomegaly, enlarged cervical lymph nodes, and a white blood count of 5,000 with 12 per cent polymorphonuclear leucocytes, 20 per cent eosinophiles, 33 per cent monocytes, and 33 per cent lymphocytes. Eight months later he had his first bout of polyarthritis, slight pigmentation of the skin, and a white cell count of 4,600 with 1.5 per cent polymorphonuclear leucocytes, 6 per cent esoinophiles, 58 per cent monocytes, and 33 per cent lymphocytes. Subsequently, he had bouts of polyarthritis every twenty-one days, lasting seven days, with a maximum depression of the neutrophiles on the third and fourth days of the bout; at times this amounted to a complete agranulocytosis, a concomitant monocytosis, and a persistent eosinophilia. During the neutropenia the bone marrow showed a shift to the left with promyelocytes predominating; during remission the marrow was normal. Two years after onset of this picture a splenectomy was performed which was followed by severe arthritis and a temporary leucocytosis. Three weeks later the neutropenia was as severe as before. The spleen showed a chronic inflammatory hyperplasia with eosinophilia of the pulp and hyperplasia of the lymph follicles. Gradually, the symptoms abated and were further improved by penicillin. At present, five years after onset of symptoms, occasional joint pains and fever recur and the neutropenia persists.

One month after the onset of symptoms an aortic insufficiency was noted. The blood pressure ranged around 150/75. A chest x-ray film showed an aortic configuration of the heart. X-ray films of the joints were normal.

The authors emphasize that the picture described by Felty is a syndrome and not a disease. They believe that the various rheumatic diseases represent varying individual reactions. The type of reaction depends on the virulence of the infecting organism and on the resistance of the body. A majority of valvular deformities found on necropsy are thought to be the result of an atypical verrucous endocarditis, rather than of the classical rheumatic endocarditis.

LENEL-PEKELIS.

Mercier, F.: Bio-Assay of Adonis Vernalis Glycosides. Cardiologia **12**:211, 1947-1948.

The author determined the minimal lethal dose in relation to the speed of administration of the two glycosides, adonidoside and adonivernoside, as well as that of a mixture of the two (adoverne), by the continuous intravenous infusion method in dogs anesthetized with chloralose. If death was produced in thirty minutes, the minimal lethal dose was 0.7 mg. per kilogram for adonidoside, 1.75 mg. per kilogram for adnivernoside, and 1.14 mg. per kilogram for adoverne. If death was delayed for two to four hours, the results were quite variable for adonidoside, indicating its rapid fixation in the myocardium and a variable rate of destruction in the organism. The minimal lethal dose of adonivernoside, on the other hand, showed a constant variation with the length of infusion, changing to 0.88 mg. per kilogram in one and one-half hours and to 0.94 mg. per kilogram in four hours. This demonstrates a slow myocardial fixation and stability in the body. With the same technique for ouabain and digitaline (Nativelle), ouabain was found to behave in a way very similar to adonidoside, while digitaline showed the same constant variation in toxicity as adonivernoside. In the slow perfusion of adoverne, adonivernoside is apparently more active than the other glycoside.

LENEL-PEKELIS.

Pattani, F.: Wolff-Parkinson-White Syndrome. Cardiologia **12**:247, 1947-1948.

The author presents three cases in which he studied the hemodynamic effects of the syndrome as well as the effect of various drugs on the abnormal complexes. Cardiac output and minute volume were normal in these patients. There was no dissociation of the ventricular systole and no kymographic abnormalities. Quinidine abolished the abnormal complexes. Sympatol, Veritol, caffeine, Coramine, dehydroergotamine, atropine, and strophanthin had no influence on the abnormal complexes. Carotid sinus pressure and change in position could induce the appearance of abnormal complexes, although this occurred at times spontaneously. Increased vagal tone is an important factor for the appearance of the abnormal complexes. This is illustrated by one case in which these complexes appeared only during the bradycardic phase of respiratory arrhythmia.

The author suggests that quinidine depresses the fibers of an abnormal muscle bundle connecting auricle and ventricle, while an increase in vagal tone depresses normal conduction and hence induces the abnormal spread of the impulse.

LENEL-PEKELIS

Franck, C., Grandpierre, R., Lemaire, R., and Auscher, C.: Action of Hyperoxygenation on the Hypertension and Hyperglycemia Induced by Adrenalin. Compt. rend. Soc. de biol. **142**:372, 1948.

In a previous communication, these authors described observations which indicate that during anoxemia the effect of adrenalin is diminished with respect to producing hyperglycemia and hypertension. In this connection they report results of experiments designed to test the effect of hyperoxemia. In a typical experiment following the injection of 0.1025 mg. adrenalin intravenously, the blood sugar rose 18 per cent and the systolic blood pressure, from 170 to 230 mm. Hg, when the oxygen concentration of the blood was 89 per cent; after inducing hyperoxemia, and when the oxygen concentration of the blood was 100 per cent, a similar dose of adrenalin raised the blood sugar only 3 per cent and the systolic blood pressure from 150 to 190 mm. of mercury. Four similar experiments are reported in detail, two of which also showed that these effects are independent of small variations in plasma carbon dioxide content.

SEGALL.

Cooper, F. W., Jr., Harris, M. H., and Kahn, J. W.: Ligation and Division of the Abdominal Aorta for Metallic Embolus From the Heart: Post-operative Observations of the Circulation in the Extremities. Ann. Surg. **127**:1 (Jan.), 1948.

The authors report an unusual instance of a 22-year-old soldier who was shot through the left arm and chest by a bullet from a 45 caliber pistol. After a period of several weeks, the bullet travelled from the heart to the lower abdominal aorta. There were episodes of severe abdominal pain and evidence of circulatory insufficiency in the lower extremities. The patient was operated upon approximately six months following injury; the lower abdominal aorta was exposed and the bifurcation of the aorta resected. The vessel was completely blocked by the foreign body and its surrounding thrombus, which was partially organized. The common iliac arteries were ligated with 00 braided silk. The aorta proximally was occluded by means of two ligatures of double braided silk and a transfixion suture. Postoperatively, there was evidence of improvement in the circulation to the lower extremities in spite of the fact that no sympathectomy or sympathetic blocks had been done. Reflex spasm from the lower abdominal aorta was considered to have initiated preoperatively some of the spasmodic effects seen in the lower extremities. After having recovered from the operation, the patient was able to walk greater distances without tiring than before the operation.

LORD.

Pick, J., and Wertheim, H.: Technique for Blocking the Carotid Sinus Nerves. Ann. Surg. **127**:144 (Jan.), 1948.

The authors described in detail a method by which the nerves arising from the carotid sinus and extending cephalad posterior to the carotid arteries may be blocked by Novocain. They have carried out the procedure in fifty patients and, other than the occurrence of a transient Horner's syndrome and hoarseness in approximately 15 per cent of these patients, no complications have been observed.

LORD.

Cunningham, G. J.: Intestinal Lesions in Malignant Hypertension With Report of a Case. Brit. M. J. **1**:1075 (Jan. 5), 1948.

Pathologic studies of widespread arteriolar lesions in hypertension have been made. Fishberg (1934) reported that the vessels of the gastrointestinal tract were involved in 9 per cent, while Moritz and Oldt (1937) found involvement in 15 per cent. The clinical picture produced by such lesions, though known, has not been reported extensively.

The case of a 44-year-old woman admitted to the hospital with headache, nausea, and vomiting is described. Examination revealed papilledema, cardiac enlargement, and a blood pressure of 270/170. Hematuria and rectal bleeding soon followed. Her course was steadily down hill. The blood urea was 100 mg. per cent. She died in coma about four weeks after admission.

Post-mortem examination of the ileum showed superficial ulceration in areas of hemorrhagic mucosa. On microscopic examination the arterioles of the submucosa showed diminution of the lumen by intimal fibrosis, well-marked fibrinoid degeneration of the vessel wall, and, in some vessels, disruption of vessel wall with surrounding inflammatory reaction.

The widespread nature of vascular change in hypertension has been known for some time. These vascular lesions are occasionally found in patients without hypertension, but severe lesions were never seen in the gastrointestinal tract or kidney in control groups. Severe lesions in the splenic arterioles, however, occur red in the control group, and their presence in hypertensive patients must be considered less significant.

WAGNER.

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SCIENTIFIC COUNCIL

At the December 13th meeting of the Board of Directors the selection of the following physicians to positions in the Scientific Council, its Executive and Research Committees, was announced:

OFFICERS

Chairman: Arlie R. Barnes, Rochester, Minn.; Vice-Chairman: Carl J. Wiggers, Cleveland; Secretary: Lowell Rantz, San Francisco.

EXECUTIVE COMMITTEE

Kenneth G. Kohlstaedt, Indianapolis; Irvine H. Page, Cleveland; Irving S. Wright, New York; Daniel C. Elkin, Atlanta; Norman E. Freeman, San Francisco; Mortimer F. Mason, Dallas; Richard Ashman, New Orleans; Eugene B. Ferris, Jr., Cincinnati; Rustin McIntosh, New York.

RESEARCH COMMITTEE

Ann G. Kuttner, New York; Francis C. Wood, Philadelphia; Lewis Thomas, New Orleans; Howard B. Sprague, Boston; Harland G. Wood, Cleveland; Robert H. Bayley, Oklahoma City; Howard B. Burchell, Rochester, Minn.; Myron Prinzmetal, Los Angeles; Eugene A. Stead, Jr., Durham; Harry Goldblatt, Los Angeles; Louis N. Katz, Chicago.

The Chairman of each Council or Section automatically becomes a member of the Executive Committee of the Scientific Council, and the Chairman of the Research Study Committees of each Council or Section automatically becomes a member of the Research Committee of the Scientific Council.

Each Council or Section of the Association will elect a Research Study Committee from its members. All matters concerning research in the field of interest of the Council or Section will be referred to its Research Study Committee for evaluation and recommendation to the Research Committee of the Scientific Council. All matters concerning research in cardiovascular disease not specifically covered by special Councils or Sections will be referred directly to the Research Committee.

Members of the Research Committee and Research Study Committees will be eligible for research grants. However, their applications will be reviewed directly by the Executive Committee of the Scientific Council.

AMERICAN COUNCIL ON RHEUMATIC FEVER

Dr. Rustin McIntosh, Director of the Pediatric Service, Presbyterian Hospital, New York, N. Y., was elected Chairman of the American Council on Rheumatic Fever of the American Heart Association at the Council's meeting in New York December 3 of last year. Dr. McIntosh also is Carpentier Professor of Pediatrics at the College of Physicians and Surgeons, Columbia University.

Mr. Lawrence J. Linck, Executive Secretary for National Society of Crippled Children and Adults, Chicago, was elected Vice-Chairman.

Newly elected members of the Council's Executive Committee include, in addition to Dr. McIntosh, Dr. Hugh McCulloch, Chicago; Dr. Walter Bauer, Boston; Dr. David D. Rutstein, Boston; Dr. Edward Harmon, Valhalla, N. Y.; Dr. M. J. Shapiro, Minneapolis; Dr. T. Duckett Jones, New York; Dr. Homer F. Swift, New York; Dr. George M. Wheatley, New York.

The following chairmen were appointed to head newly created committees: Dr. Ann Kuttner, New York, Chairman, Research Study Committee; Dr. Wheatley, Chairman, Committee on Community Rheumatic Fever Programs; Dr. Rutstein, Chairman, Committee on Standards and Criteria for Programs of Care; Dr. H. M. Marvin, Chairman, Membership Committee; Dr. Francis F. Schwentker, Chairman, Committee on Education and Training.

A committee headed by Dr. T. Duckett Jones will assume responsibility for the rheumatic fever portion of the program of the International Congress on Rheumatic Diseases, which will be held in New York May 30 to June 2.

It was agreed that within the framework of the policies of the American Heart Association, responsibility for all activities related to rheumatic fever and rheumatic heart disease should be assigned as heretofore to the American Council on Rheumatic Fever. These activities include the stimulation, guidance, coordination, and sponsorship of the following:

1. Research along laboratory, clinical, and epidemiological lines in accordance with an approved agreement of interrelationship among: (a) Executive bodies of the American Heart Association, (b) Research Committee of the Scientific Council, and (c) American Council on Rheumatic Fever.

2. Education of the medical profession and other professional groups at all levels—undergraduate, graduate, and postgraduate.

3. Public Health aspects of rheumatic fever and rheumatic heart disease, including establishment of standards for facilities necessary for community programs; complete collection of accurate vital statistics; the employment of patients with rheumatic fever and rheumatic heart disease; the planning and coordination of case-finding efforts; cooperation with existing voluntary and governmental agencies; and the performance of any studies necessary for the accomplishment of the above.

4. Health education of the public.

5. Establishment of a clearing house for information concerning the activities in the field of rheumatic fever and rheumatic heart disease in cooperation with governmental and other agencies.

In order to carry out this program the American Council on Rheumatic Fever accepts the responsibility for the conduct of the rheumatic fever program of the American Heart Association. This will include the following:

1. Preparation of a budget covering all expenditures in the rheumatic fever program.
2. Recommendation of number and qualifications of staff personnel.
3. Planning and guidance of studies related to rheumatic fever.
4. Authorization to make recommendations through its own Research Study Committee concerning the expenditure of funds allocated for research on rheumatic fever and rheumatic heart disease.

The Council recommends further that the allocation of research funds among various fields with which the American Heart Association is or may hereafter become concerned be determined by the Board of Directors of the American Heart Association subsequent to recommendations of the appropriate Committee of the Scientific Council of the Association. Such recommendations should be determined by the relative opportunities for advancement of knowledge in the various fields and not on any fixed, predetermined percentage basis. In order that such policy be effective, each of the sections or councils of the American Heart Association should have appropriate representation on that Committee of the Scientific Council of the American Heart Association.

AMERICAN FOUNDATION FOR HIGH BLOOD PRESSURE RESEARCH

The representatives of both groups, in a previous meeting in Cleveland, were unanimous in the opinion that they should merge, so that the Foundation could continue its work within the structure of the American Heart Association, to avoid duplication of effort and conflict in fund-raising activities.

The plan for the merger recognizes two phases of the merger: first, the steps necessary to complete the merger; and second, those necessary to set up a procedure for use during the interim period in which the Foundation will transfer its functions to the Association and wind up its affairs as a separate entity.

The Foundation's functions will be transferred to a Section of the Heart Association's Scientific Council. This will be known as the Section of Hypertension. As a Section of the Scientific Countil it will be entitled to the same rights and privileges as the other sections of the Council.

The plan for functioning during the interim period includes:

1. Recognition of the existing Research Study Committee of the Foundation, if agreeable to the Foundation.
2. Reference of all matters concerning research in the field of hypertension to this Committee for its evaluation and recommendation.
3. Appointment of its Chairman to the Research Committee of the Scientific Council.
4. Representation of the Foundation on all important and relevant committees and a voice in all discussions relating to hypertension during the interim period.

The American Heart Association will prepare a letter approving the fund-raising efforts of the Foundation on an interim basis until the merger of the two organizations is complete. In cities in which the Foundation and a local Heart Association are conducting campaigns, the letter will urge the cooperation of the two groups. In cities where a joint effort will be made by the two groups during the interim period, agreements for the division of funds derived as a result of a joint campaign shall be made by the local groups. These agreements should recognize the 70/30 allocation fraction of the American Heart Association, as well as the specific commitment to research of funds received by the Foundation. It is felt that these agreements can only be worked out effectively on the local level.

In San Francisco, Los Angeles, and Cincinnati where the American Heart Association will not conduct a campaign in 1949, the Foundation will proceed with its campaign with the approval of the American Heart Association.

In all other cities an attempt will be made to conduct a joint campaign. It is understood that the measure of cooperation in each city will vary and that the plan for the joint conduct of a campaign will be a local matter.

The problem of coordinating campaigns of the two organizations during the interim period is a difficult one. It is recognized by both organizations that it is highly desirable to conduct one campaign wherever possible. However, it is understood that this can only be done by agreements between the two local groups. Both organizations pledge themselves to assist and encourage their local groups to set up cooperative campaigns.

REPORT ON AFFILIATED HEART ASSOCIATIONS

The following Heart Associations have been accepted by the Association for affiliation for 1949:

Chicago Heart Association
Children's Heart Association of Rhode Island
Heart Council of Greater Cincinnati
Illinois Heart Association
Indiana Heart Foundation
Maryland Rheumatic Fever and Heart Association
Miami Heart Association
Minnesota Heart Association
New York Heart Association
New England Heart Association
Philadelphia Heart Association
Texas Heart Association
Washington Heart Association
Washington State Heart Association
Wisconsin Heart Association
California Tuberculosis and Health Association
Heart Committee of Onondaga Health Association
Central Ohio Heart Association
Louisiana Heart Association
Missouri Heart Association
New Jersey Heart Association
Oregon Heart Association
St. Louis Heart Association
Tulsa County Heart Association
Youngstown Area Heart Association
Cleveland Heart Association
Iowa Heart Association
Waterbury Heart Association
West Virginia Heart Association
Georgia Heart Association

Committee on Heart Disease and Rheumatic Fever of the Tuberculosis and Health Association of Rochester and Monroe County, Inc.

DR. JOHN W. FERREE DIRECTS PUBLIC HEALTH DIVISION

Dr. John W. Ferree has assumed his new duties as Director of the Association's Public Health Division. Dr. Ferree has served as Associate Director of the National Health Council since April, 1947.

Dr. Ferree has a wide background in public health. In 1946 and 1947 he was Director of the Division of Educational Services of the American Social Hygiene Association. Previously, he served as Commander in charge of the VD Control Section, Division of Preventive Medicine, Bureau of Medicine and Surgery, Navy Department, Washington, D. C.

In 1940 Dr. Ferree became State Health Commissioner in Indiana, and in 1942 he became Secretary of the Association of State and Territorial Health Officers.

As Director of the Association's Public Health Division, Dr. Ferree will have the assistance of a staff to prepare program and educational materials, and field workers trained in health work who will engage in community organization and program development. The Division will aid heart associations or local committees in developing effective health programs. It will work closely with the newly organized National Conference of Executive Secretaries.

Dr. Ferree will represent the Association on councils, committees, conferences, and assemblies concerned with public health matters that hold significance for the Association. Experienced public health physicians will be included on such advisory committees as may be appropriate for developing and carrying out program and policies assigned to or initiated by the Division.

ROME A. BETTS APPOINTED EXECUTIVE DIRECTOR

Rome A. Betts is now serving as Executive Director of the Association. He has been General Secretary of the American Bible Society since 1942.

Mr. Betts has figured prominently in national service organizations as well as in local civic and welfare activities. He is a member of the City Council of Summit, N. J., and was President of the U.S.O.-United Campaign there in 1942. He has been a leader both in local and national Y.M.C.A. activities and is President of the Protestant Film Commission. He became Associate Secretary of the American Bible Society in 1937.

1949 NATIONAL CAMPAIGN

Harold E. Stassen, National Chairman, was scheduled to open the Association's 1949 campaign with a radio address from Boston over a nationwide radio hookup on February 7. Dr. Tinsley R. Harrison, President of the Association, was to be heard on the same program along with the governors of several New England states.

Campaign leaders announced since the last issue of the JOURNAL include: Maurice Tobin, U. S. Secretary of Labor, as Chairman of the Labor Committee of the Heart Campaign; Mark Woods, President of the American Broadcasting Company, as Chairman of the Public Relations Committee; and Irene Dunne, film star, as Chairman of the Women's Committee.

A precampaign luncheon for business and corporation executives was held at the University Club in New York on January 12. Among the guests were Mr. Stassen and Dr. Leonard A. Scheele, Surgeon General of the U. S. Public Health Service. The meeting was also attended by members of the Association's Board of Directors and the campaign planning and sponsors' committees.

AMENDMENTS TO BY-LAWS

The Association's Board of Directors has approved amendments to the By-Laws providing that each affiliated local Heart Association with less than one million residents in its territory will be entitled to elect two delegates to the Assembly. Affiliates with more than a million residents are entitled to two delegates for each additional million or fraction.

Provision also was made for the election of ten delegates-at-large from each of the six geographic regions in the United States and Canada. Delegates will serve for a term of two years, and their terms will be staggered so that elections are held each year.

Each of the following groups will elect annually five delegates to the Assembly: Scientific Council, American Council on Rheumatic Fever, Section on Circulation, and Section on Hypertension.

The Board of Directors, consisting of forty members, will include the President, President-Elect, Vice-President, and Treasurer. Twenty-four members are to be elected by the full Assembly. At least two directors must be elected from each geographic region.

At its annual meeting each year the Board of Directors will elect an Executive Committee of not more than fifteen directors, including the President and President-Elect.

DR. VAN SLYKE ON ASSEMBLY

Dr. C. J. Van Slyke, Director of the National Heart Institute of the U. S. Public Health Service, has been elected to the Assembly of the Association.

SWISS CARDIOLOGICAL SOCIETY FORMED

The formation of the Swiss Cardiological Society, with Dr. Ivan Mahaim, President, Dr. Max Holzmann, Vice-President, and Dr. Pierre W. Duchosal, Secretary, was recently announced. Two meetings will take place every year. The first will be held in May concurrently with that of the Swiss Society of Internal Medicine, with which the Cardiological group is connected. The second meeting will be held in November.